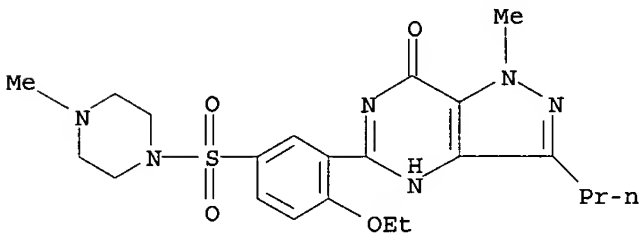
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 139755-83-2 REGISTRY
CN Piperazine, 1-[[3-(4,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Pyrazolo[4,3-d]pyrimidine, piperazine deriv.
OTHER NAMES:
CN 5-[2-Ethoxy-5-(4-methyl-1-piperazinylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one
CN **Sildenafil** VIAGRA
FS 3D CONCORD
MF C22 H30 N6 O4 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

389 REFERENCES IN FILE CA (1962 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
393 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=>

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=> file reg; d stat que l10
FILE 'REGISTRY' ENTERED AT 14:29:26 ON 16 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:   15 JUL 2002  HIGHEST RN 438572-95-3
DICTIONARY FILE UPDATES:  15 JUL 2002  HIGHEST RN 438572-95-3

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf


L8                STR
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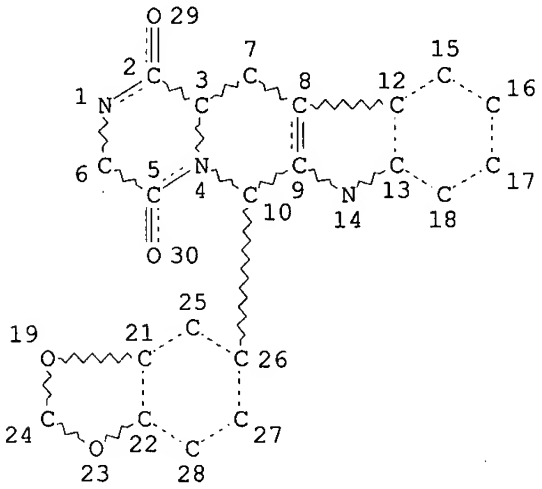


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
L10          178 SEA FILE=REGISTRY SSS FUL L8

100.0% PROCESSED    189 ITERATIONS                    178 ANSWERS
SEARCH TIME: 00.00.01


=> file caplus; d que nos l11; d que nos l12
FILE 'CAPLUS' ENTERED AT 14:30:16 ON 16 JUL 2002
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FILE COVERS 1907 - 16 Jul 2002 VOL 137 ISS 3
FILE LAST UPDATED: 15 Jul 2002 (20020715/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L10         178 SEA FILE=REGISTRY SSS FUL L8
L11          38 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10
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L12          37 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND PHARMAC?/SC,SX
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=> d ibib abs hitstr l12 1-37

L12  ANSWER 1 OF 37  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:427673  CAPLUS
DOCUMENT NUMBER:          137:3711
TITLE:                    Cells and animals homozygous or heterozygous for a
                          knockout of the PDE11A gene and their uses
INVENTOR(S):              Burslem, Martin F.; Harrow, Ian Dennis; Lanfear,
                          Jeremy; Phillips, Stephen C.
PATENT ASSIGNEE(S):       Pfizer Limited, UK; Pfizer Inc.
SOURCE:                   Eur. Pat. Appl., 31 pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ----------------  ----  --------      ---------------  --------
     EP 1211313         A2   20020605      EP 2001-308959   20011022
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
```

PRIORITY APPLN. INFO.: GB 2000-26727 A 20001101
GB 2001-11710 A 20010514

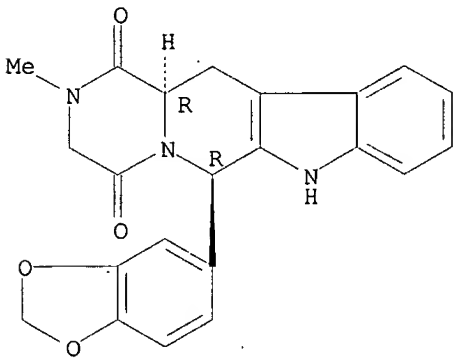
AB Animal cells and animals carrying a knockout of the gene for the cyclic nucleotide phosphodiesterase PDE11 are described for use in anal. of the role of the enzyme, esp. in spermatogenesis and in the screening of drugs for regulation of spermatogenesis. Heterozygous knockout mice show lowered levels of spermatogenesis. The effect of the knockout on patterns of gene expression was analyzed by microarray hybridization. Known inhibitors of cyclic nucleotide phosphodiesterases were tested for their ability to inhibit PDE11. The pattern of inhibition was similar to, but distinct from, that for PDE5. Array hybridization was used to analyze the effects of PDE11 knockout on gene expression in testis. Twenty-four genes (18 down-regulated and 6 up-regulated) were identified. These gene products may themselves be therapeutic targets for PDE11-related disease (no data).

IT **171596-29-5**, IC-351
RL: PAC (Pharmacological activity); BIOL (Biological study)
(as inhibitor of PDE11; cells and animals homozygous or heterozygous for knockout of PDE11A gene and their uses)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:391540 CAPLUS
DOCUMENT NUMBER: 136:380144
TITLE: Phosphodiesterase V inhibitors for the treatment of premature ejaculation
INVENTOR(S): Boolell, Mitradev
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002040027 | A1 | 20020523 | WO 2001-IB2180 | 20011119 |

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002091129 A1 20020711 US 2001-990955 20011116
PRIORITY APPLN. INFO.: GB 2000-28245 A 20001120
US 2001-260564P P 20010109

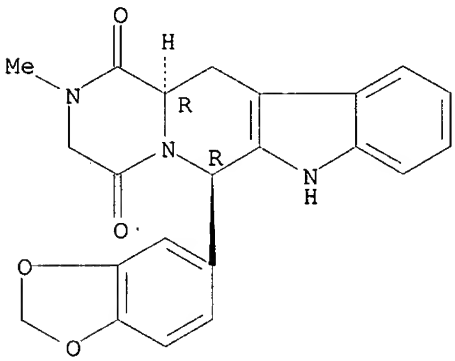
AB The invention relates to the use of cGMP phosphodiesterase V inhibitors, including in particular the compd. sildenafil, for the treatment of premature ejaculation in patients with normal erectile function.

IT **171596-29-5**, IC 351
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase V inhibitors for treatment of premature ejaculation)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

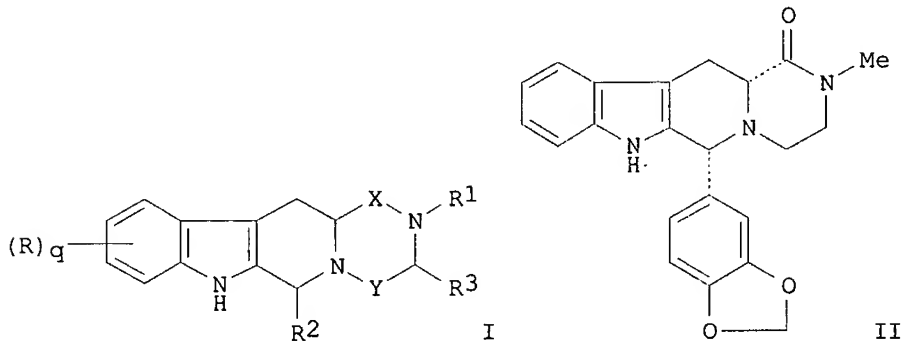
L12 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:353456 CAPLUS
DOCUMENT NUMBER: 136:369739
TITLE: Preparation of pyrazino[1',2':1,6]pyrido[3,4-b]indole derivatives as phosphoesterase inhibitors for use as therapeutic agents
INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.
PATENT ASSIGNEE(S): Lilly Icos L.L.C., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002036593 | A1 | 20020510 | WO 2001-US31364 | 20011009 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-246257P P 20001106
OTHER SOURCE(S): MARPAT 136:369739
GI

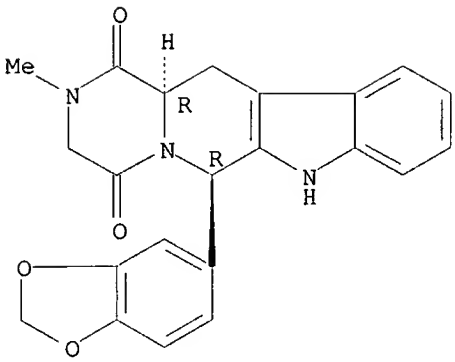



AB 2,3,6,7,12,12A-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole derivs., such as I [R = halo, alkyl; R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, heteroarylalkyl, etc.; R2 = monocyclic arom. ring, such as benzene, thiophene, furan, pyridine, etc.; R3 = H, alkyl; R1,R3 = fused carbocyclic ring; X, Y = CO, SO, SO2, CS, C(Ra)2; Ra = H, alkyl, benzyl; q = 0-4], pharmaceutically acceptable salts and solvates thereof, were prepd. for pharmaceutical use as phosphodiesterase inhibitors for the treatment of conditions, such as erectile dysfunction, female arousal disorder, angina, hypertension, and vascular disease. Thus, pyrazinopyridoindole deriv. II was prepd. by a multistep procedure starting with D-Tryptophan Me ester, piperonal and chloroacetaldehyde. The prepd. heterocycles were tested for phosphodiesterase V (PDE5) inhibitory activity with II exhibiting an IC50 of 54 nM.

IT **171596-29-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pyrazino[1',2':1,6]pyrido[3,4-b]indole derivs. as phosphoesterase inhibitors for use as therapeutic agents)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:241329 CAPLUS
DOCUMENT NUMBER: 136:284433
TITLE: Administration of phosphodiesterase inhibitors for the treatment of premature ejaculation
INVENTOR(S): Wilson, Leland F.; Doherty, Paul C.; Place, Virgil A.; Smith, William L.; Abdel-Hamid, Abdou Ali Ibrahim Aboubakr
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 467,094.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002037828 | A1 | 20020328 | US 2001-888250 | 20010621 |
| US 6403597 | B2 | 20020611 | | |
| US 6037346 | A | 20000314 | US 1998-181070 | 19981027 |

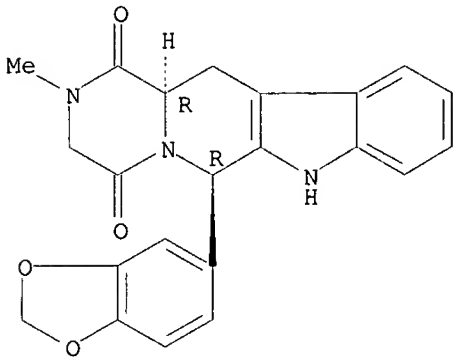
PRIORITY APPLN. INFO.: US 1997-958816 B2 19971028
US 1998-181070 A2 19981027
US 1999-467094 A2 19991210

AB A method is provided for treatment of premature ejaculation by administration of a phosphodiesterase inhibitor, e.g., an inhibitor of a Type III, Type IV, or Type V phosphodiesterase. In a preferred embodiment, administration is on as "as needed" basis, i.e., the drug is administered immediately or several hours prior to sexual activity. Pharmaceutical formulations and packaged kits are also provided. Zaprinast 1.0, mannitol 1.0, microcryst. cellulose 2.0, and magnesium stearate 10 mg are blended in a suitable mixer and then compressed into sublingual tablets. Each sublingual tablet contains 10 mg zaprinast.

IT **171596-29-5**, GF 196960
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GF 196960; administration of phosphodiesterase inhibitors for treatment of premature ejaculation)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:142493 CAPLUS
DOCUMENT NUMBER: 136:194255
TITLE: Treatment of the insulin resistance syndrome
INVENTOR(S): Fryburg, David Albert; Gibbs, Earl Michael; Koppiker, Nandan Parmanand
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002013798 | A2 | 20020221 | WO 2001-IB1428 | 20010806 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
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| AU 2001076607 | A5 | 20020225 | AU 2001-76607 | 20010806 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2000-224928P | P | 20000811 |
| GB 2000-30649 | A | 20001215 |
| US 2001-266083P | P | 20010202 |
| GB 2001-6465 | A | 20010315 |
| GB 2001-6468 | A | 20010315 |
| GB 2001-17134 | A | 20010713 |
| WO 2001-IB1428 | W | 20010806 |

AB Use of a selective cGMP PDE5 inhibitor or a pharmaceutical compn. thereof in the prepn. of a medicament for the curative, palliative or prophylactic treatment of the insulin resistance syndrome wherein the insulin resistance syndrome means the concomitant existence in a subject of two or more of: dyslipidemia; hypertension; type 2 diabetes mellitus, impaired glucose tolerance (IGT) or a family history of diabetes; hyperuricemia and/or gout; a pro-coagulant state; atherosclerosis; or truncal obesity wherein said use can occur alone or in combination with other agents to treat the insulin resistance syndrome or individual aspects of the insulin

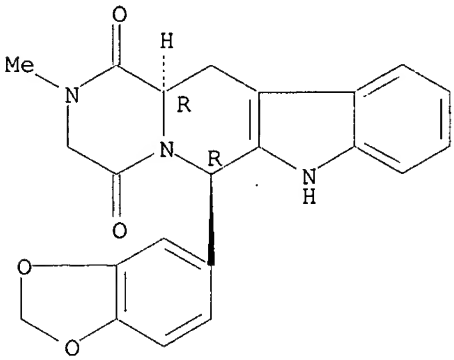
resistance syndrome.

IT **171596-29-5**, IC-351
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of the insulin resistance syndrome)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:122770 CAPLUS

DOCUMENT NUMBER: 136:178015

TITLE: Drugs for incontinence - salified and nonsalified nitric oxide-donors and phosphodiesterase inhibitors

INVENTOR(S): Del Soldato, Piero; Benedini, Francesca

PATENT ASSIGNEE(S): Nicox S.A., Fr.

SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002011707 | A2 | 20020214 | WO 2001-EP8734 | 20010727 |
| W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001091691 | A5 | 20020218 | AU 2001-91691 | 20010727 |

PRIORITY APPLN. INFO.: IT 2000-MI1848 A 20000808
WO 2001-EP8734 W 20010727

OTHER SOURCE(S): MARPAT 136:178015

AB Use in the incontinence of one or more of the following classes of drugs selected from the following: (B) salified and nonsalified nitric oxide-donor drugs, of formula: A - X1 - N(O)z, (B') nitrate salts of drugs used for the incontinence, and which do not contain in the mol. a nitric oxide donor group; (C) org. or inorg. salts of compds. inhibiting

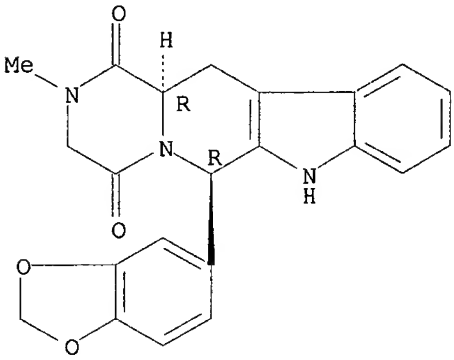
phosphodiesterases.

IT **171596-29-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salified and nonsalified nitric oxide-donors and phosphodiesterase inhibitors for treatment of incontinence)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




L12 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:107344 CAPLUS
DOCUMENT NUMBER: 136:151441
TITLE: Preparation of fused heterocyclic derivatives as phosphodiesterase inhibitors
INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.
PATENT ASSIGNEE(S): Lilly Icos L.L.C., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002010166 | A1 | 20020207 | WO 2001-US21678 | 20010709 |

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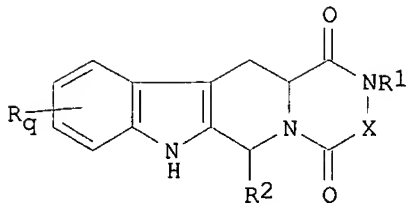
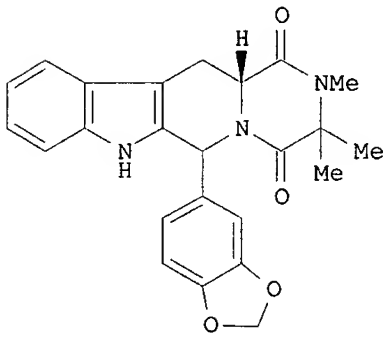
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-222451P P 20000802
OTHER SOURCE(S): MARPAT 136:151441
GI



I



II

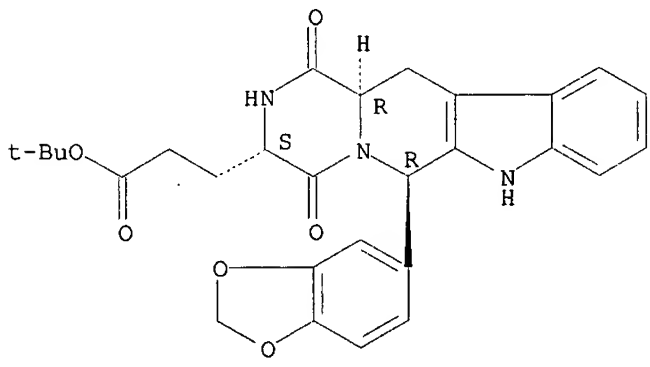
AB Compds. I [R = halo, alkyl; q = 0-4; R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, cycloalkylalkyl, arylalkyl, heteroarylalkyl; R2 is an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine or an optionally substituted bicyclic ring; X = NH or substituted imino, O, S, substituted methylene or ethylene; the substituents may form addnl. rings] and their salts and solvates were prepd. for use as phosphodiesterase (PDE) inhibitors. Thus, compd. II was prepd. by a multistep procedure starting with coupling of L-tryptophan Me ester with CbzNMeCMe2CO2H (Cbz = benzyloxycarbonyl) and showed IC50 = 161.0 nM for inhibition of cGMP-PDE.

IT **395665-39-1P 395665-40-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of fused heterocyclic derivs. as phosphodiesterase inhibitors)

RN 395665-39-1 CAPLUS

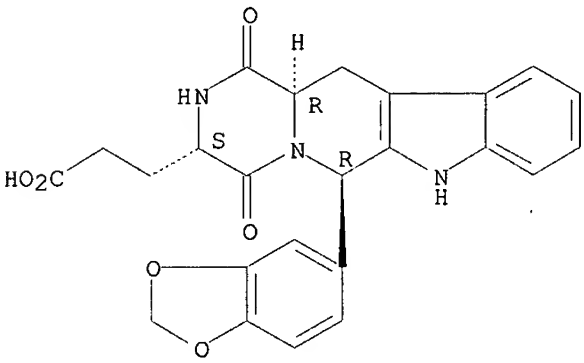
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 395665-40-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

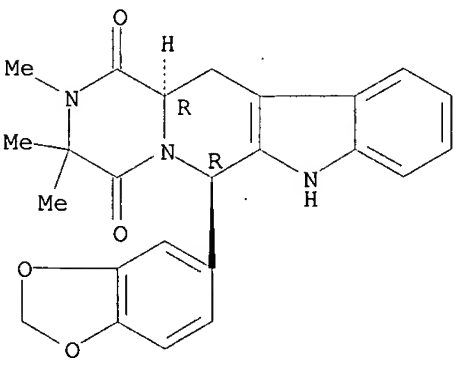
Absolute stereochemistry. Rotation (+).



IT **395665-35-7P 395665-36-8P 395665-41-5P**
**395665-42-6P 395665-43-7P 395665-47-1P**
**395665-49-3P 395665-51-7P 395665-53-9P**
**395665-55-1P 395665-57-3P 395665-59-5P**
**395665-61-9P 395665-63-1P 395665-65-3P**
**395665-67-5P 395665-69-7P 395665-70-0P**
**395665-71-1P 395665-72-2P 395665-73-3P**
**395665-75-5P 395665-76-6P 395665-77-7P**
**395665-78-8P 395665-79-9P 395665-80-2P**
**395665-81-3P 395665-91-5P 395665-95-9P**
**395665-96-0P 395665-98-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of fused heterocyclic derivs. as phosphodiesterase inhibitors)

RN 395665-35-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3,3-trimethyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

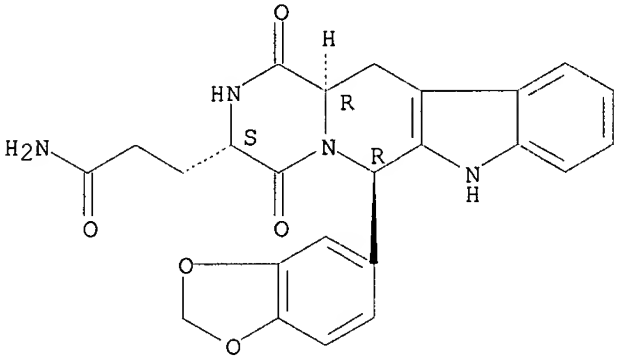
Absolute stereochemistry.



RN 395665-36-8 CAPLUS

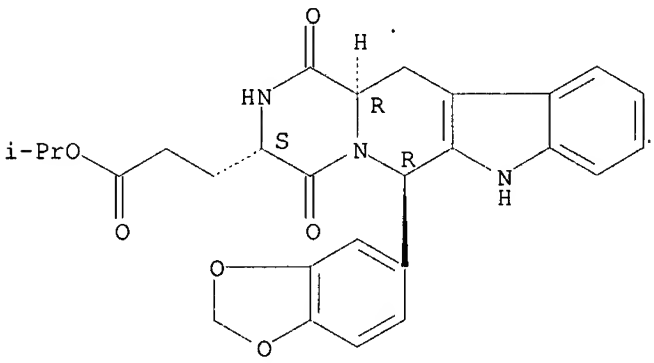
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



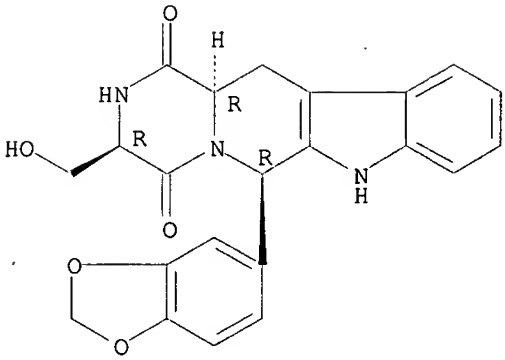
RN 395665-41-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1-methylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



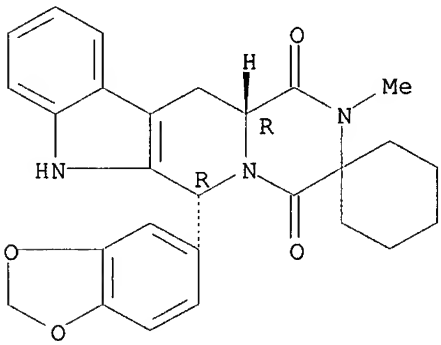
RN 395665-42-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(hydroxymethyl)-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



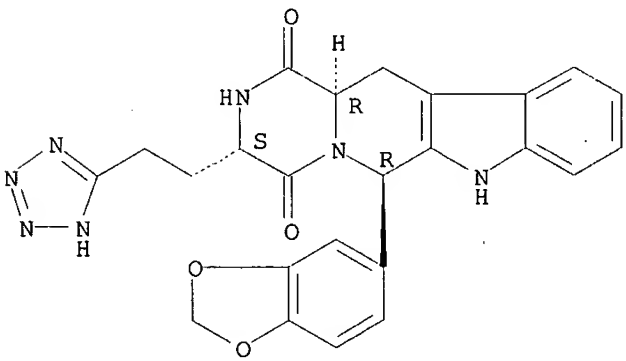
RN 395665-43-7 CAPLUS
CN Spiro[cyclohexane-1,3'(4'H)-pyrazino[1',2':1,6]pyrido[3,4-b]indole]-1',4'(2'H)-dione, 6'-(1,3-benzodioxol-5-yl)-6',7',12',12'a-tetrahydro-2'-methyl-, (6'R,12'aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-47-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-[2-(1H-tetrazol-5-yl)ethyl]-, (3S,6R,12aR)-(9CI) (CA INDEX NAME)

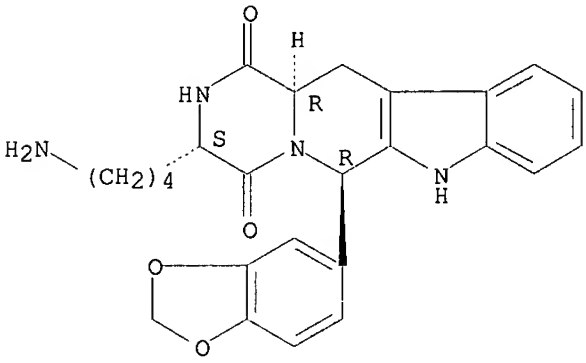
Absolute stereochemistry.



RN 395665-49-3 CAPLUS

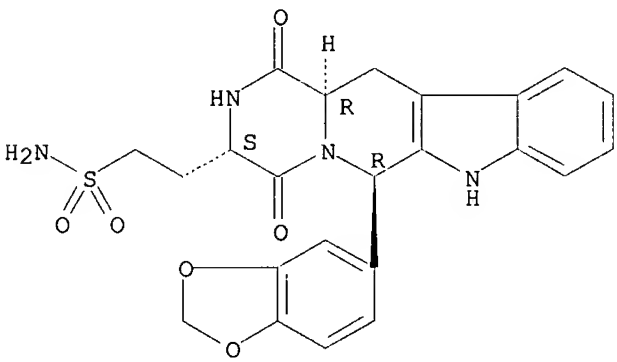
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 3-(4-aminobutyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



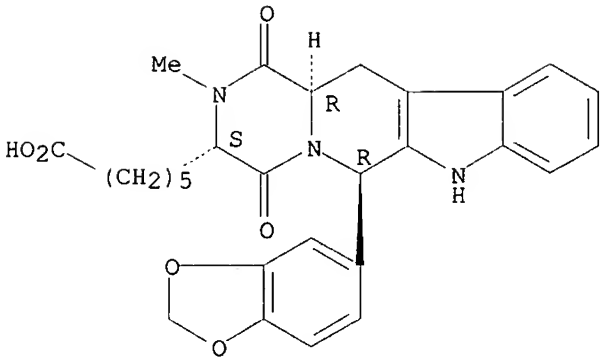
RN 395665-51-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-ethanesulfonamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



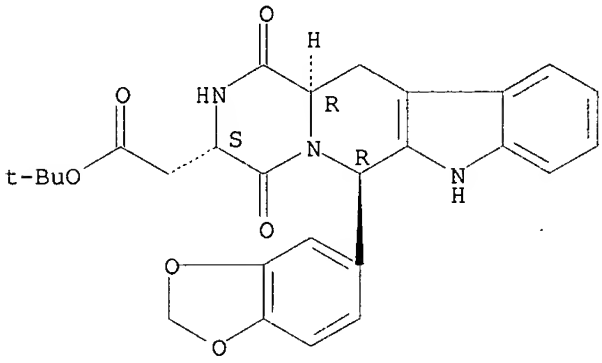
RN 395665-53-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-hexanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



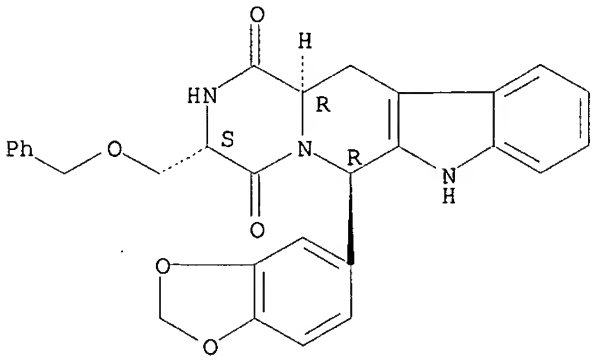
RN 395665-55-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-57-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-[(phenylmethoxy)methyl]-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

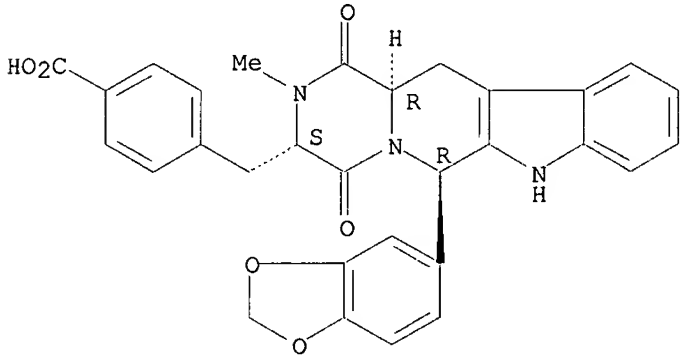
Absolute stereochemistry.



RN 395665-59-5 CAPLUS

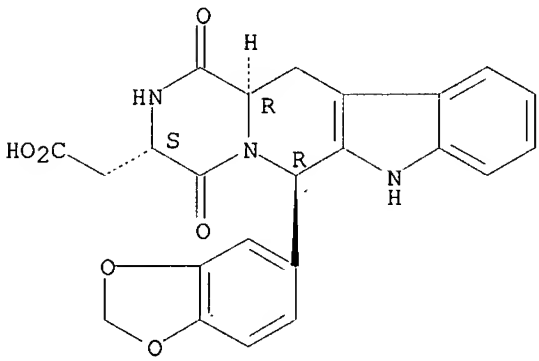
CN Benzoic acid, 4-[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



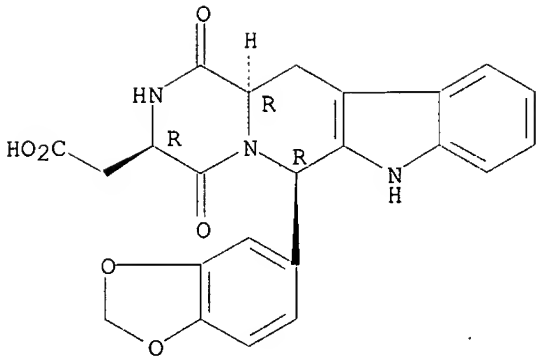
RN 395665-61-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



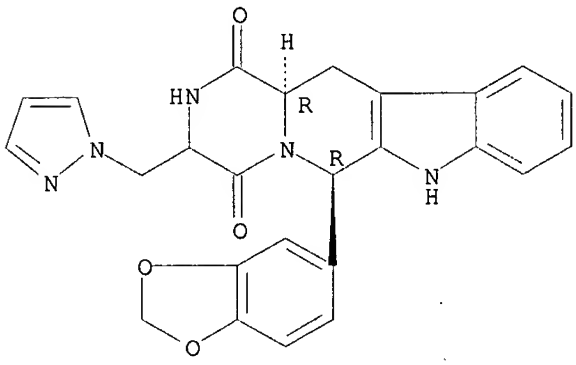
RN 395665-63-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



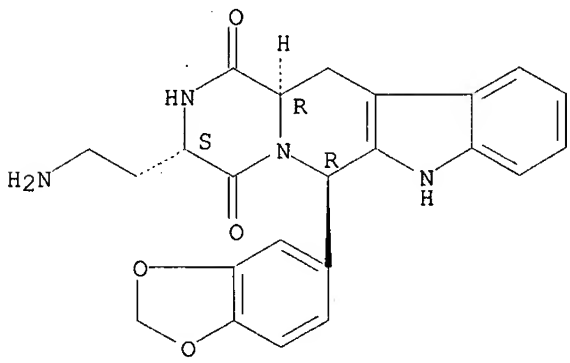
RN 395665-65-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(1H-pyrazol-1-ylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-67-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 3-(2-aminoethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

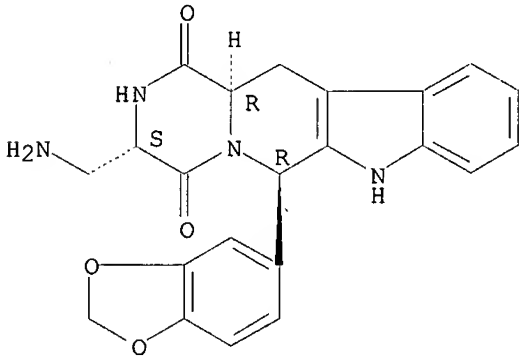
Absolute stereochemistry.



RN 395665-69-7 CAPLUS

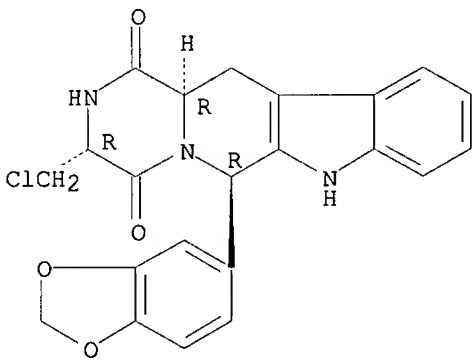
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 3-(aminomethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



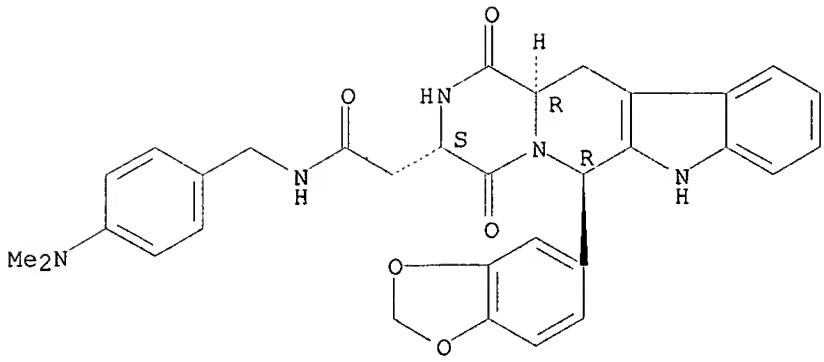
RN 395665-70-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-3-(chloromethyl)-2,3,6,7,12,12a-hexahydro-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



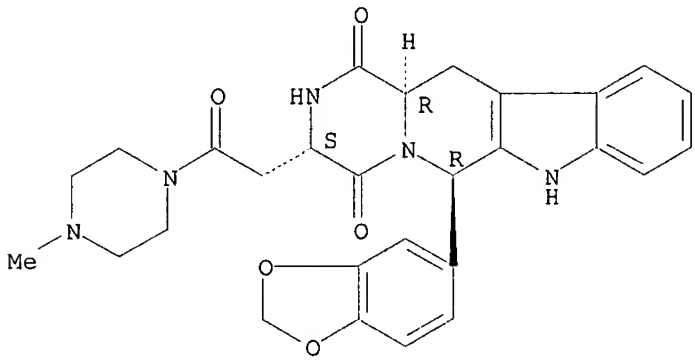
RN 395665-71-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetamide, 6-(1,3-benzodioxol-5-yl)-N-[[4-(dimethylamino)phenyl]methyl]-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



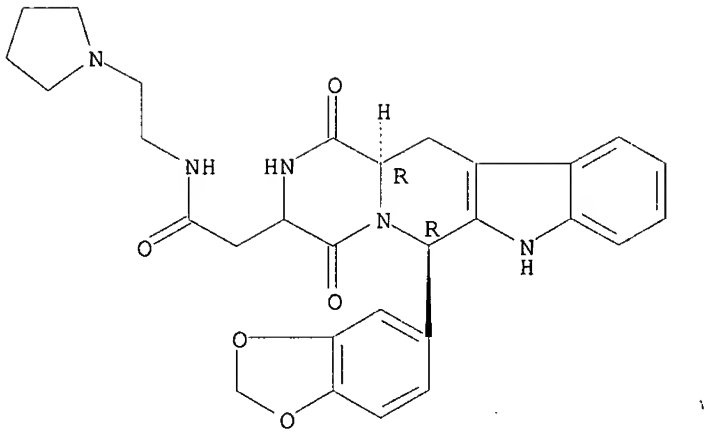
RN 395665-72-2 CAPLUS
CN Piperazine, 1-[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]acetyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



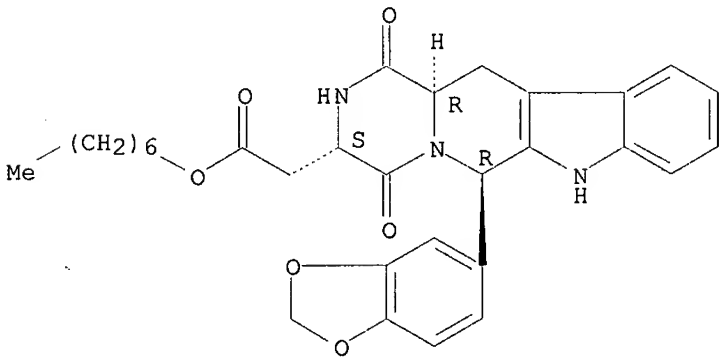
RN 395665-73-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-N-[2-(1-pyrrolidinyl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



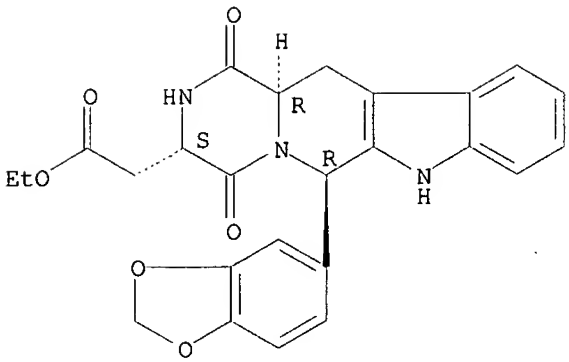
RN 395665-75-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, heptyl ester, (3S,6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



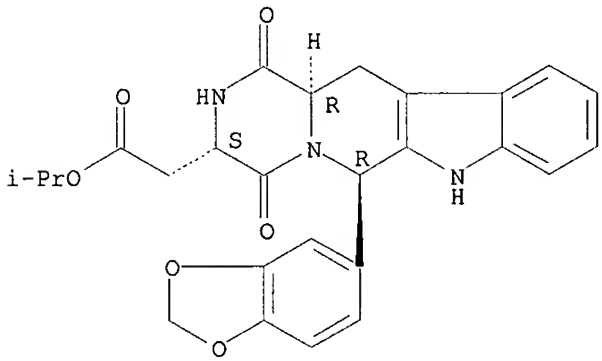
RN 395665-76-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, ethyl ester, (3S,6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



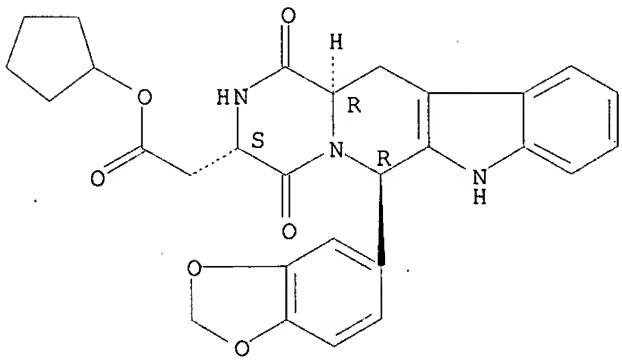
RN 395665-77-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1-methylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-78-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, cyclopentyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

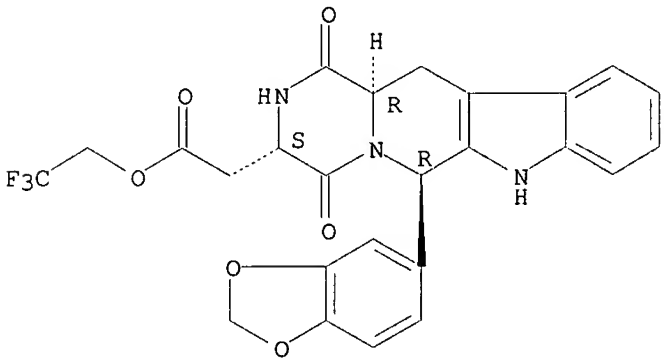
Absolute stereochemistry.



RN 395665-79-9 CAPLUS

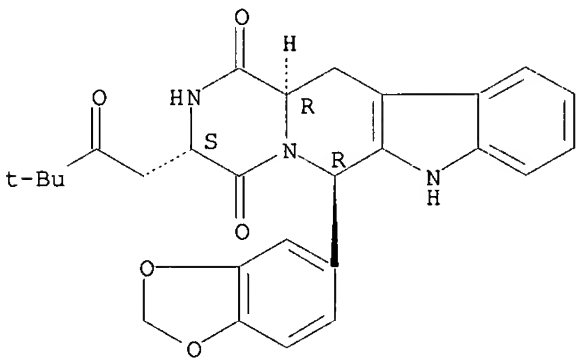
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 2,2,2-trifluoroethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



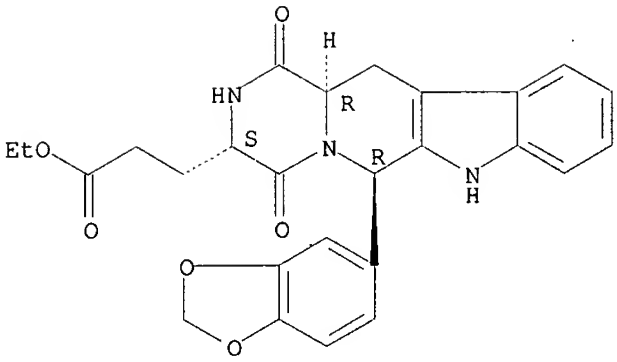
RN 395665-80-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-3-(3,3-dimethyl-2-oxobutyl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



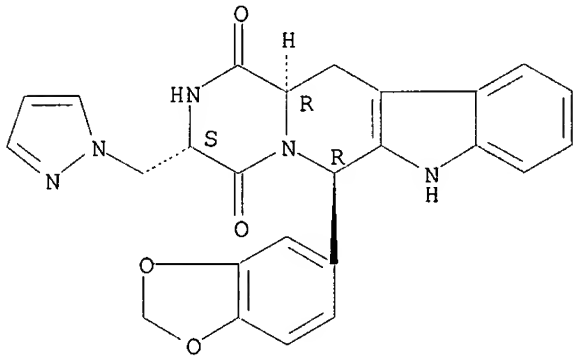
RN 395665-81-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, ethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



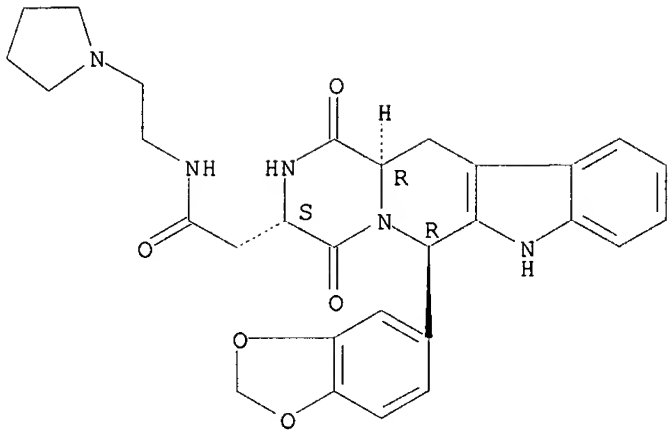
RN 395665-91-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(1H-pyrazol-1-ylmethyl)-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



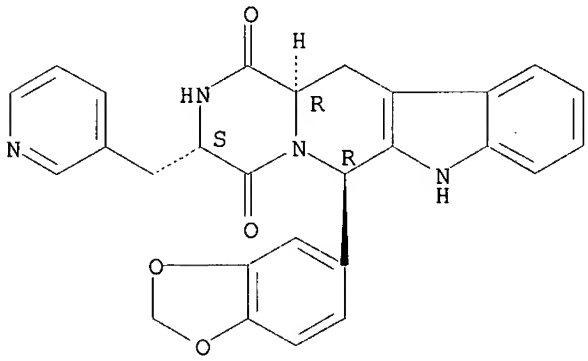
RN 395665-95-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-N-[2-(1-pyrrolidinyl)ethyl]-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



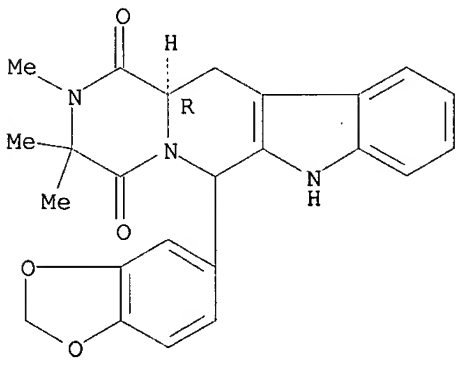
RN 395665-96-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(3-pyridinylmethyl)-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-98-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3,3-trimethyl-, (12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:51273 CAPLUS
DOCUMENT NUMBER: 136:96099
TITLE: Treatment of male sexual dysfunction
INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002003995 | A2 | 20020117 | WO 2001-IB1187 | 20010702 |
| WO 2002003995 | A3 | 20020418 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002052370 | A1 | 20020502 | US 2001-893585 | 20010628 |
| AU 2001069353 | A5 | 20020121 | AU 2001-69353 | 20010702 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| GB 2000-16684 | A | 20000706 |
| GB 2000-30647 | A | 20001215 |
| GB 2001-6167 | A | 20010313 |
| GB 2001-8483 | A | 20010404 |
| US 2000-219100P | P | 20000718 |
| GB 2001-1584 | A | 20010122 |
| US 2001-274957P | P | 20010312 |
| WO 2001-IB1187 | W | 20010702 |

OTHER SOURCE(S): MARPAT 136:96099

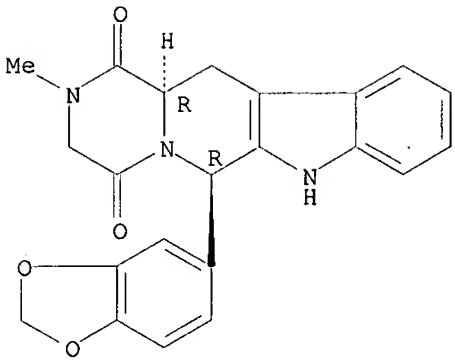
AB The present invention relates to the use of neutral endopeptidase inhibitors (NEPi) and a combination of NEPi and phosphodiesterase type (PDE5) inhibitor for the treatment of male sexual dysfunction, in particular MED.

IT **171596-29-5**, IC-351
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

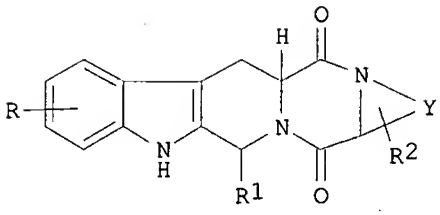


L12 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10477 CAPLUS
DOCUMENT NUMBER: 136:85829
TITLE: preparation of ring fused pyrazinopyridoindole derivatives as cyclic GMP-specific phosphodiesterase inhibitors
INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott
PATENT ASSIGNEE(S): Lilly Icos Llc, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

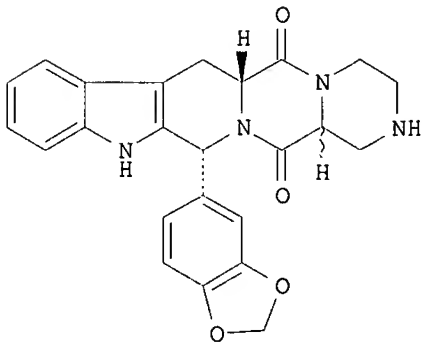
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002000658 | A1 | 20020103 | WO 2001-US16164 | 20010517 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001063278 | A5 | 20020108 | AU 2001-63278 | 20010517 |

PRIORITY APPLN. INFO.: US 2000-213651P P 20000623
WO 2001-US16164 W 20010517

OTHER SOURCE(S): MARPAT 136:85829
GI



I



II

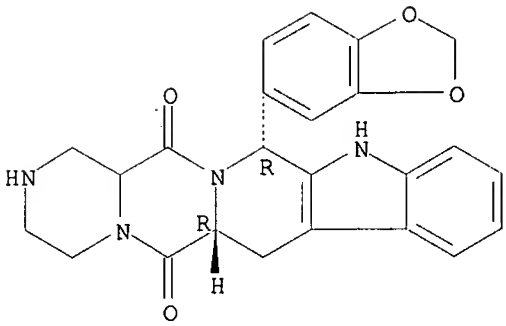
AB The title compds. I (R = halo, C1-6-alkyl; R1 = a nonocyclic arom. ring selected from benzene, thiophene, furan, and pyridine, and an optionally substituted bicyclic ring wherein the fused ring is a 5- or 6-membered ring and optionally with one or two heteroatoms selected from O, S, and N; Y = a 3-, 4-, or 5-membered carbon chain of a 5-, 6-, or 7-membered heteroatom chain of a 5-, 6-, or 7-membered unsubstituted or substituted ring wherein the heteroatom chain contains one or two heteroatoms selected from O, S, N; R2 = nitro, halo, cyano, acyl, acyloxy, C1-4-alkyleneHet, etc.) and their pharmaceutically acceptable salts were prepd. as cyclic GMP-specific phosphodiesterase inhibitors. Thus, N,N'-bis-CBZ-2-carboxypiperazine was treated with Me 1,2,3,4-tetrahydro-1-(3,4-methylenedioxyphenyl)-9H-pyrido[3,4-b]indole-3-carboxylate and the product cyclized by H2 in presence of Pd-C to give the tetraazaindenoanthracenedione II. The IC50 of II as cyclic GMP-specific phosphodiesterase inhibitor was 1.7 nM.

IT **385765-02-6P 385765-03-7P**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of ring fused pyrazinopyridoindole derivs. as cyclic GMP-specific phosphodiesterase inhibitors)

RN 385765-02-6 CAPLUS

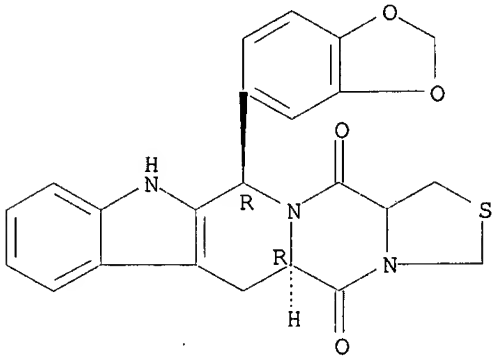
CN 6H-Pyrazino[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-6,15(2H)-dione, 13-(1,3-benzodioxol-5-yl)-1,3,4,6a,7,12,13,15a-octahydro-, (6aR,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



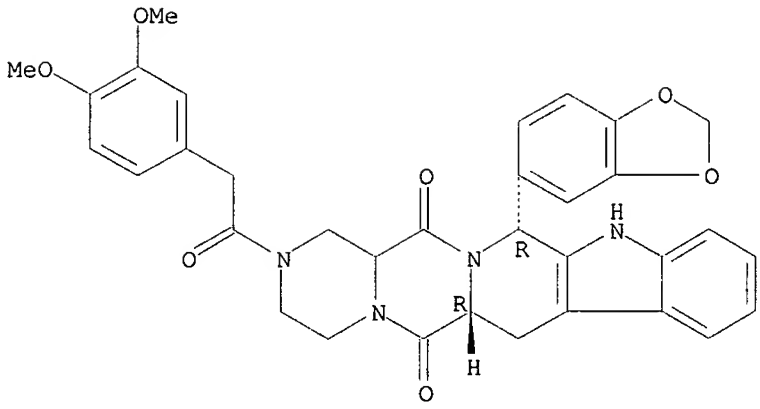
RN 385765-03-7 CAPLUS
CN 3H,5H,14H-Thiazolo[3'',4'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-5,14-dione, 12-(1,3-benzodioxol-5-yl)-1,5a,6,11,12,14a-hexahydro-, (5aR,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



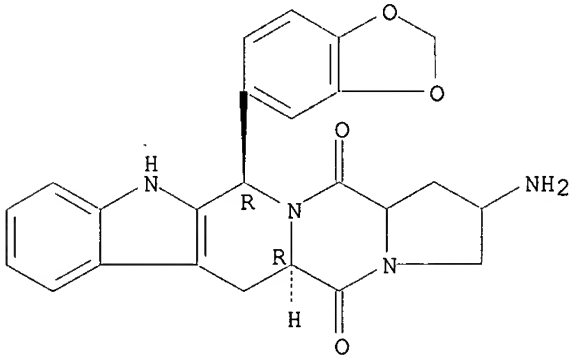
IT **385765-04-8P 385765-05-9P 385765-06-0P**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ring fused pyrazinopyridoindole derivs. as cyclic GMP-specific phosphodiesterase inhibitors)
RN 385765-04-8 CAPLUS
CN 6H-Pyrazino[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-6,15(2H)-dione, 13-(1,3-benzodioxol-5-yl)-2-[(3,4-dimethoxyphenyl)acetyl]-1,3,4,6a,7,12,13,15a-octahydro-, (6aR,13R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



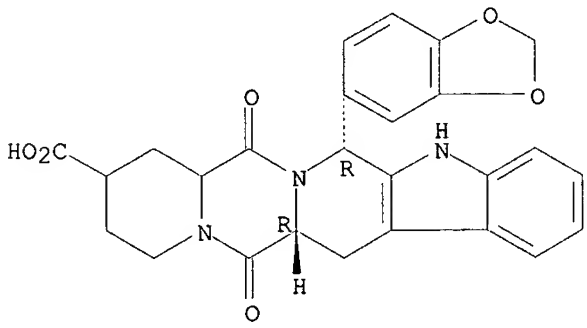
RN 385765-05-9 CAPLUS
CN 5H,14H-Pyrrolo[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-5,14-dione, 2-amino-12-(1,3-benzodioxol-5-yl)-1,2,3,5a,6,11,12,14a-octahydro-, (5aR,12R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385765-06-0 CAPLUS
CN 5H-Pyrido[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-10-carboxylic acid, 6-(1,3-benzodioxol-5-yl)-6,8,8a,9,10,11,12,14,14a,15-decahydro-8,14-dioxo-, (6R,14aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10475 CAPLUS
DOCUMENT NUMBER: 136:85828
TITLE: Preparation of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors
INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.; Daugan, Alain Claude-Marie; Gellibert, Francoise
PATENT ASSIGNEE(S): Lilly Icos LLC, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002000656 | A2 | 20020103 | WO 2001-US15935 | 20010515 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001061707 | A5 | 20020108 | AU 2001-61707 | 20010515 |

PRIORITY APPLN. INFO.: US 2000-213647P P 20000623
WO 2001-US15935 W 20010515

OTHER SOURCE(S): MARPAT 136:85828
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

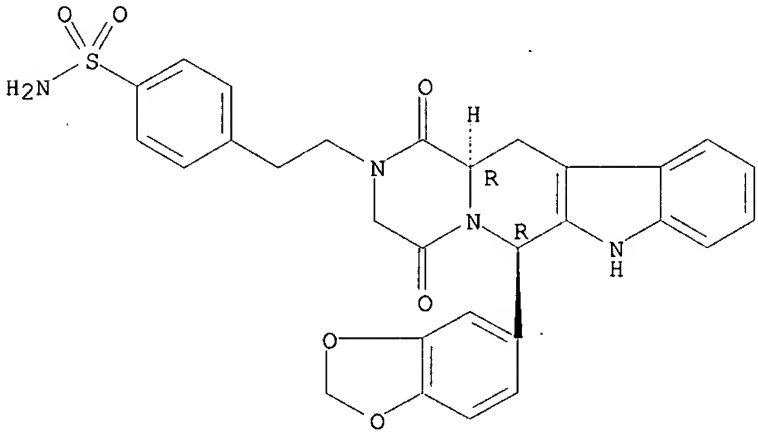
AB The pyrazinopyridoindolediones I (R = halo, C1-6-alkyl; R1 = aryl, heteroaryl, amino, R4O, R4CO, R4SO, R4SO2, C1-4-alkylene-CO2R4, C1-4-alkylenehetreroaryl, sulfamoyl, cyano, NO2, CO-C1-4-alkyleneheteroaryl, C1-4-alkylene-OR4, etc.; R2 = monocyclic arom. ring consisting of benzene, thiophene, furan, and pyridine, and an optionally substituted bicyclic ring wherein the fused ring is a 5- or 6-membered ring comprised of C and optionally heteroatoms selected from O, S, and N; R3 = H, C1-6-alkyl; R4 = H, alkyl, aryl, heteroaryl, etc.) and their salts and solvates were prepd. as cyclic GMP phosphodiesterase inhibitors. Thus, D-tryptophan Me ester hydrochloride was treated with piperonal to give the carbolinecarboxylate II, which was treated with chloroacetyl chloride followed by cyclization with hydroxylamine-HCl to give the pyrazinopyridoindoledione III. The cyclic GMP phosphodiesterase inhibitor IC50 of III 0.0075 .mu.M.

IT **385769-78-8P 385769-80-2P 385769-82-4P**
**385769-84-6P 385769-86-8P 385769-88-0P**
**385769-90-4P 385769-94-8P 385769-98-2P**
**385770-00-3P 385770-01-4P 385770-03-6P**
**385770-04-7P 385770-06-9P 385770-07-0P**
**385770-09-2P 385770-11-6P 385770-13-8P**

385770-15-0P 385770-18-3P 385770-20-7P
385770-22-9P 385770-24-1P 385770-26-3P
385770-28-5P 385770-29-6P 385770-30-9P
385770-31-0P 385770-32-1P 385770-34-3P
385770-36-5P 385770-38-7P 385770-40-1P
385770-41-2P 385770-43-4P 385770-44-5P
385770-46-7P 385770-48-9P 385770-49-0P
385770-50-3P 385770-52-5P 385770-54-7P
385770-56-9P 385770-57-0P 385770-58-1P
385770-60-5P 385770-62-7P 385770-64-9P
385770-66-1P 385770-68-3P 385770-70-7P
385770-72-9P 385770-73-0P 385770-75-2P
385770-76-3P 385770-77-4P 385770-78-5P
385770-79-6P 385770-80-9P 385770-82-1P
385770-83-2P 385770-85-4P 385770-89-8P
385770-91-2P 385770-92-3P 385770-93-4P
385770-95-6P 385770-96-7P 385770-98-9P
385770-99-0P 385771-02-8P 385771-03-9P
385771-05-1P 385771-06-2P 385771-08-4P
385771-10-8P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors)

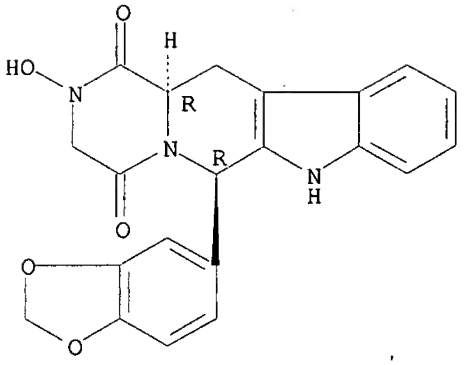
RN 385769-78-8 CAPLUS
CN Benzenesulfonamide, 4-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



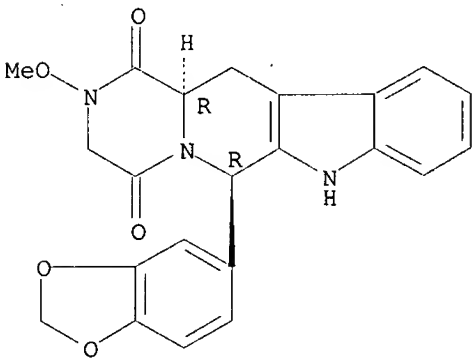
RN 385769-80-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-hydroxy-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



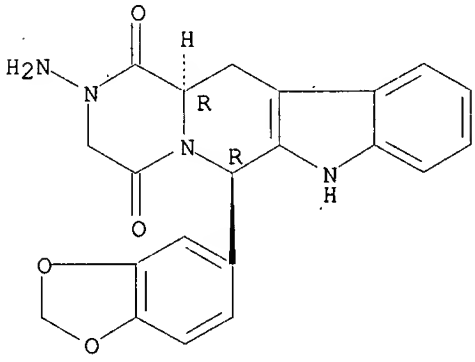
RN 385769-82-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methoxy-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385769-84-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-amino-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

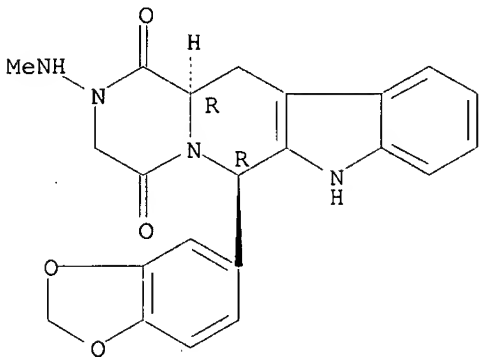
Absolute stereochemistry.



RN 385769-86-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-

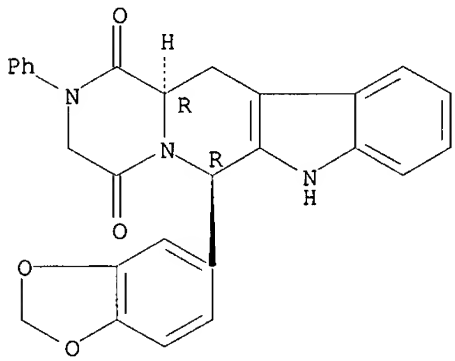
2,3,6,7,12,12a-hexahydro-2-(methylamino)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



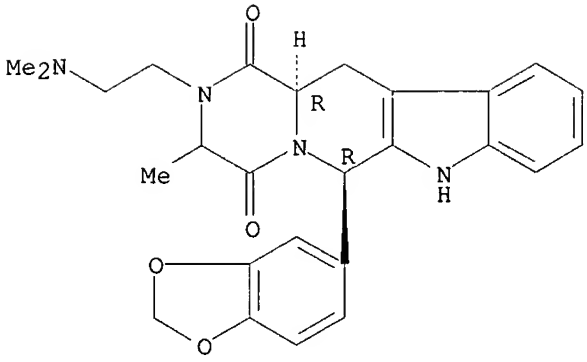

RN 385769-88-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-phenyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



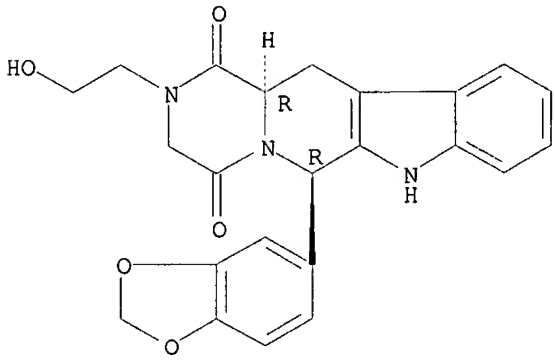

RN 385769-90-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(dimethylamino)ethyl]-2,3,6,7,12,12a-hexahydro-3-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



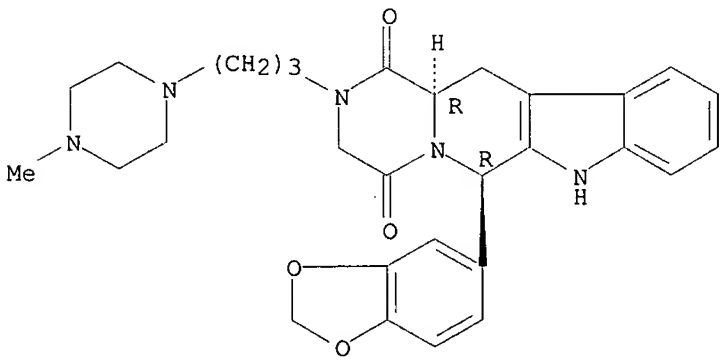
RN 385769-94-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-hydroxyethyl)-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 385769-98-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(4-methyl-1-piperazinyl)propyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

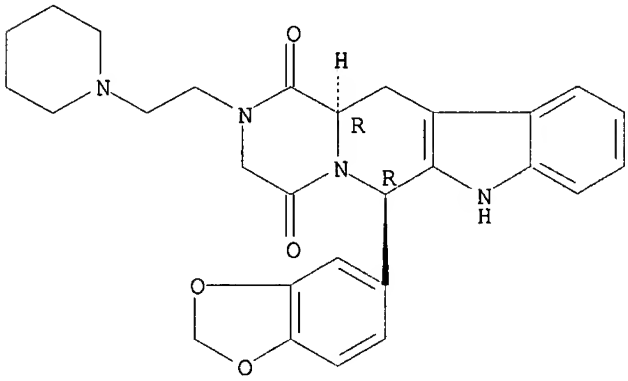
Absolute stereochemistry.



RN 385770-00-3 CAPLUS

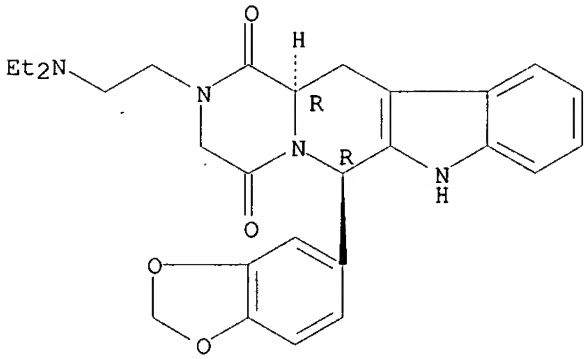
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1-piperidinyl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



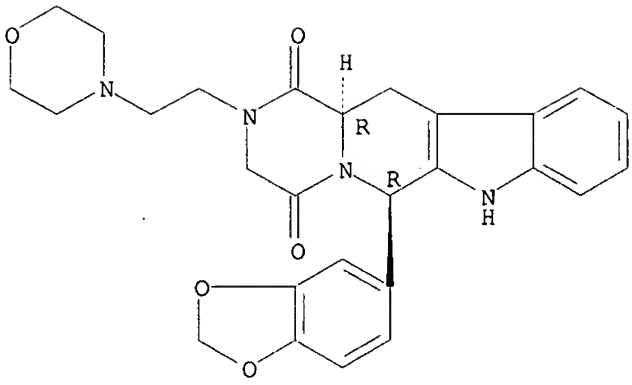
RN 385770-01-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(diethylamino)ethyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



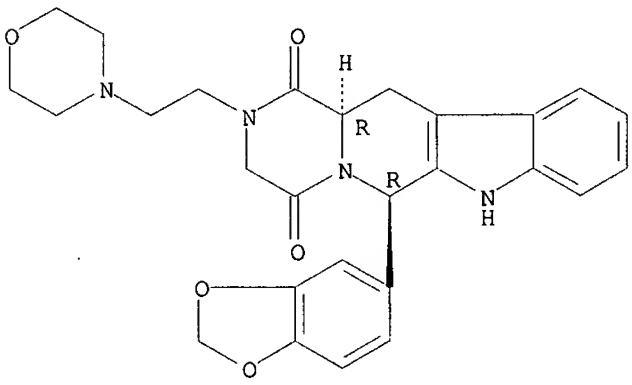
RN 385770-03-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(4-morpholinyl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



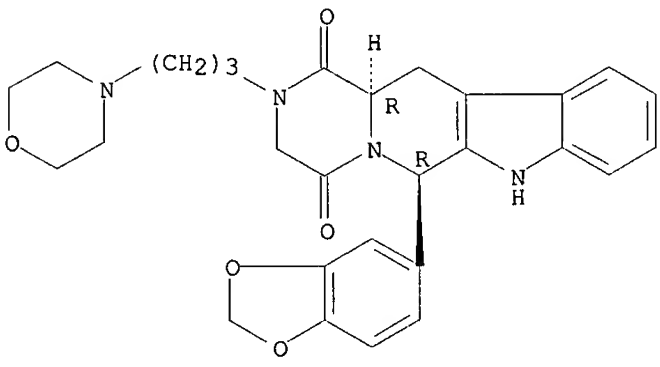
RN 385770-04-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(4-morpholinyl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



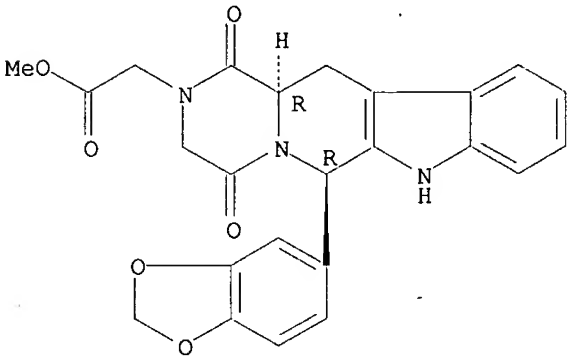
RN 385770-06-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(4-morpholinyl)propyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



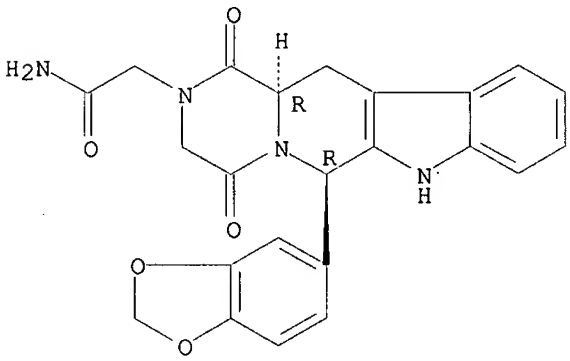
RN 385770-07-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, methyl ester, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



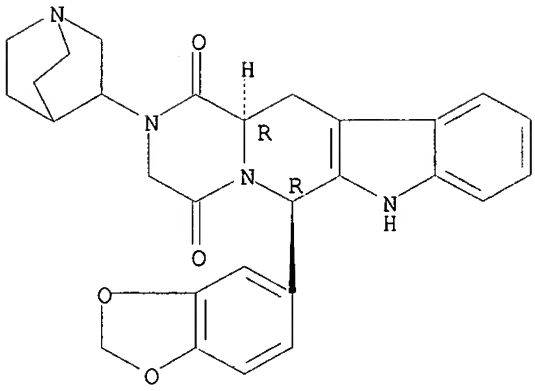
RN 385770-09-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



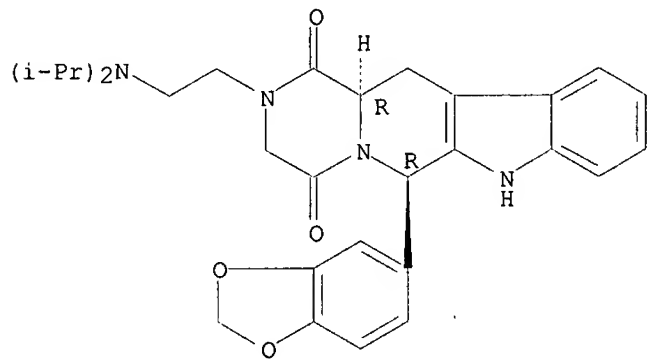
RN 385770-11-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-(1-azabicyclo[2.2.2]oct-3-yl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



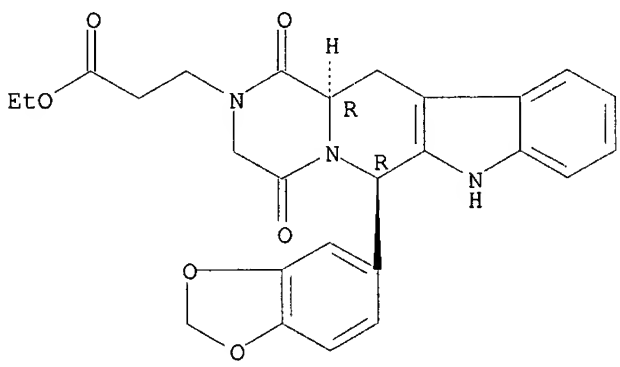
RN 385770-13-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-[bis(1-methylethyl)amino]ethyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



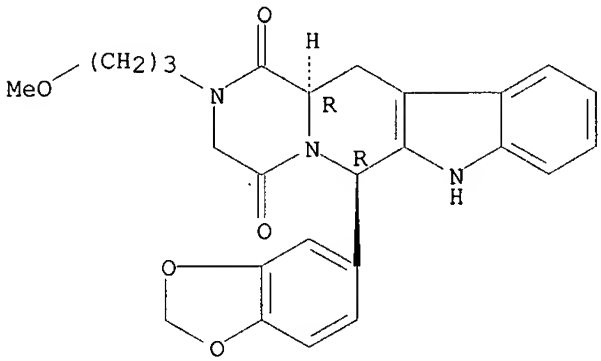
RN 385770-15-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanoic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, ethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



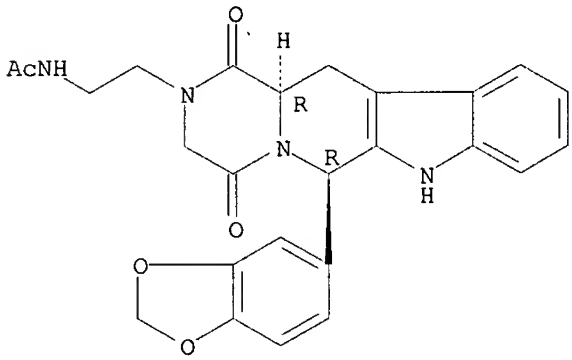
RN 385770-18-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3-methoxypropyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



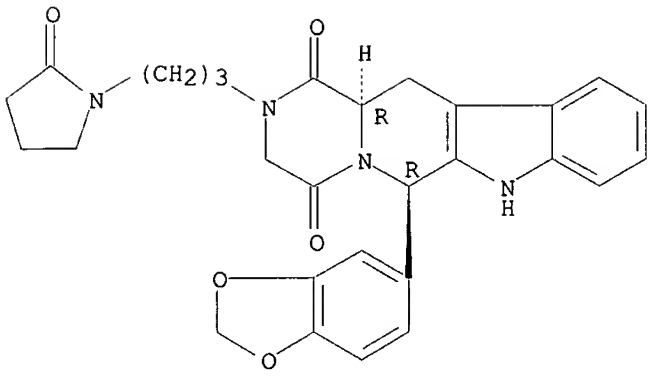
RN 385770-20-7 CAPLUS
CN Acetamide, N-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



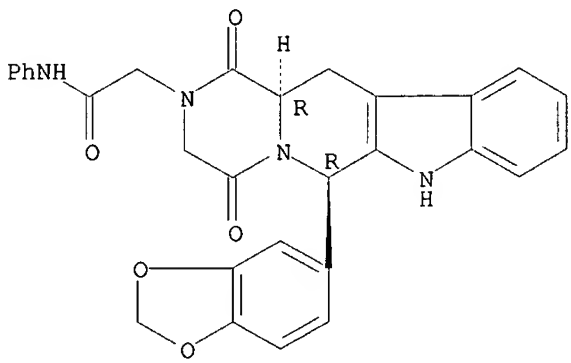
RN 385770-22-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(2-oxo-1-pyrrolidinyl)propyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



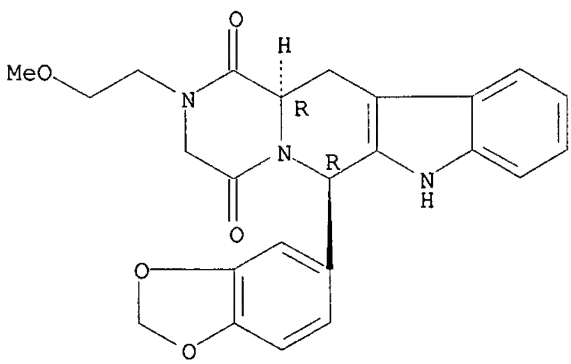
RN 385770-24-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-N-phenyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



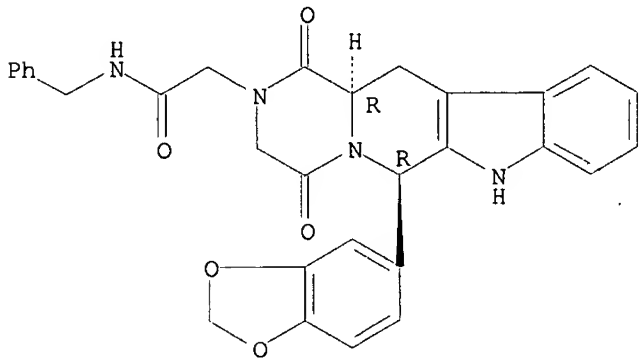
RN 385770-26-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-methoxyethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



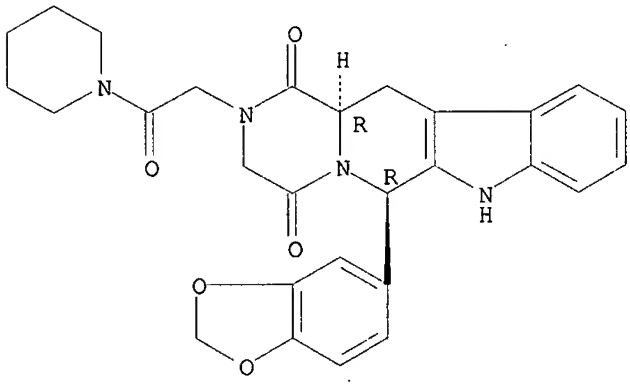
RN 385770-28-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-N-(phenylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



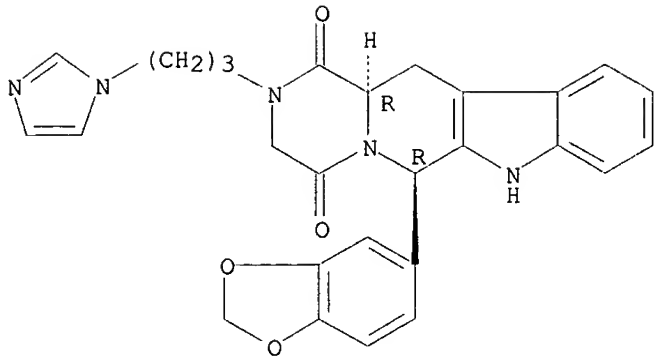
RN 385770-29-6 CAPLUS
CN Piperidine, 1-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



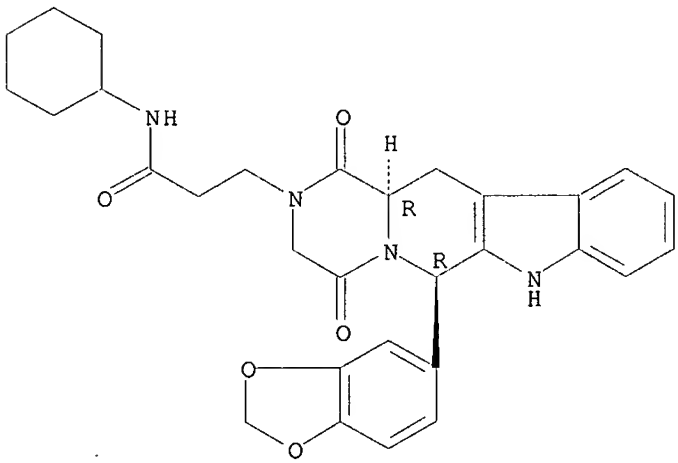
RN 385770-30-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(1H-imidazol-1-yl)propyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



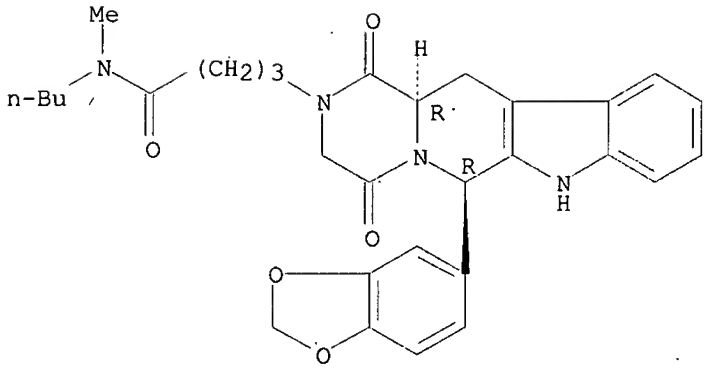
RN 385770-31-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanamide, 6-(1,3-benzodioxol-5-yl)-N-cyclohexyl-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



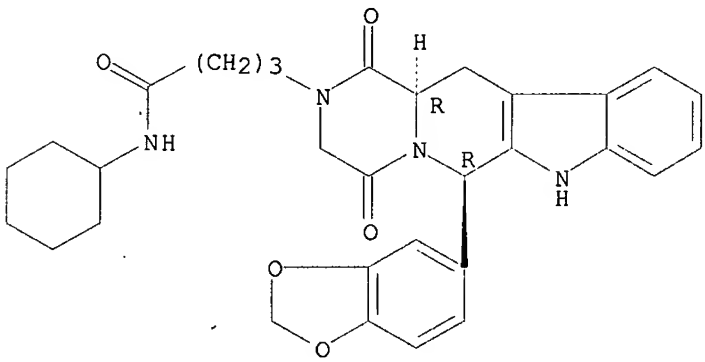
RN 385770-32-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-butanamide, 6-(1,3-benzodioxol-5-yl)-N-butyl-3,4,6,7,12,12a-hexahydro-N-methyl-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



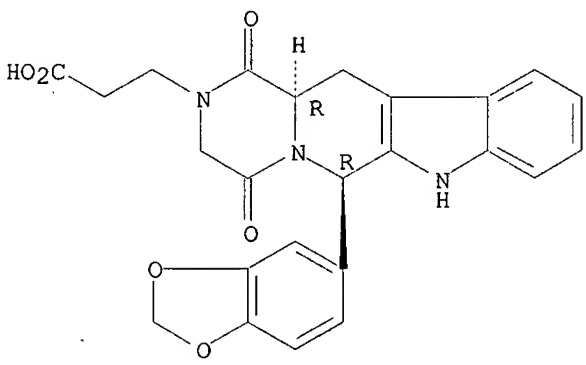
RN 385770-34-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-butanamide, 6-(1,3-benzodioxol-5-yl)-N-cyclohexyl-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



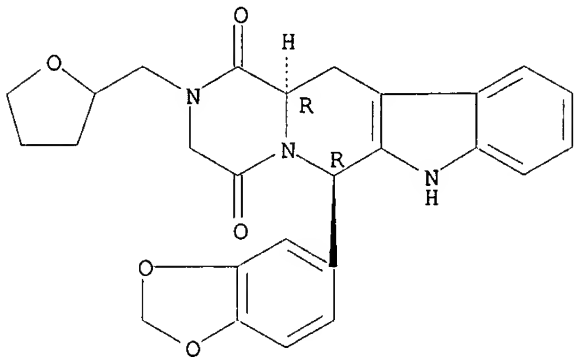
RN 385770-36-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanoic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



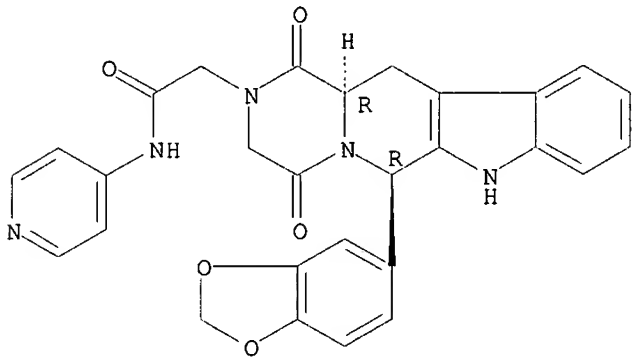
RN 385770-38-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(tetrahydro-2-furanyl)methyl]-, (6R,12aR)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.



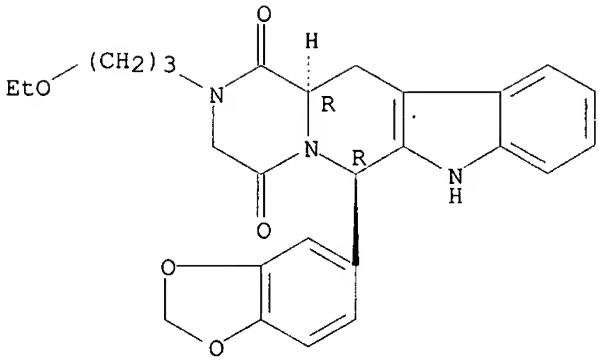
RN 385770-40-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-N-4-pyridinyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



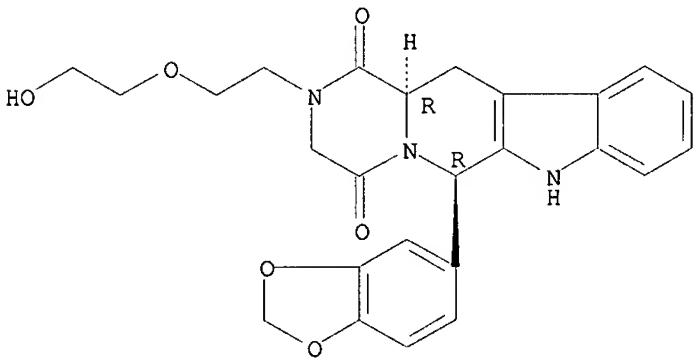
RN 385770-41-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(3-ethoxypropyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



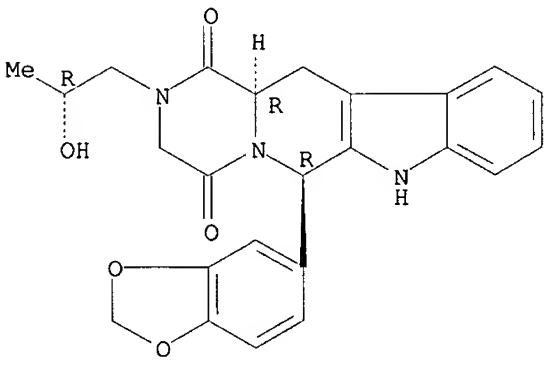
RN 385770-43-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(2-hydroxyethoxy)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385770-44-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(2R)-2-hydroxypropyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

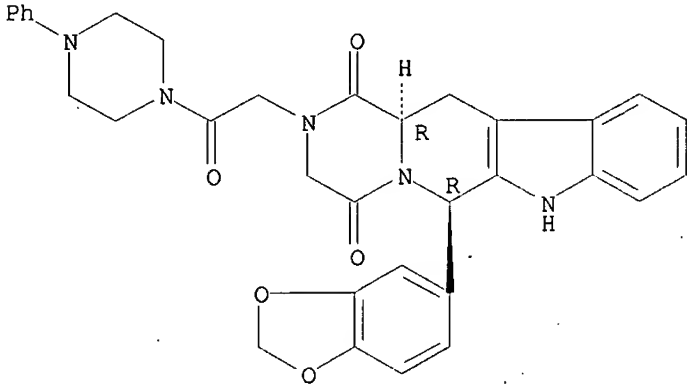
Absolute stereochemistry.



RN 385770-46-7 CAPLUS

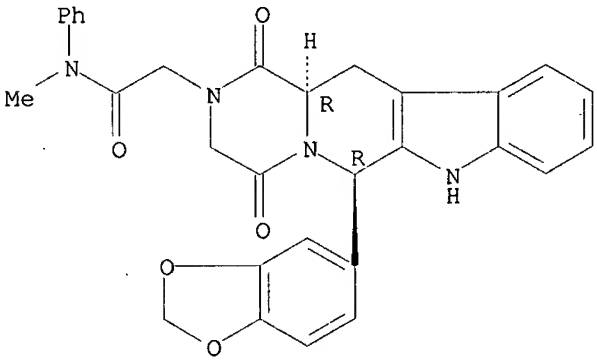
CN Piperazine, 1-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



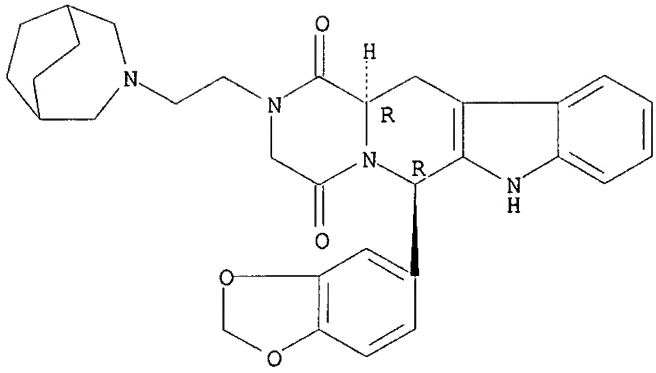
RN 385770-48-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-N-methyl-1,4-dioxo-N-phenyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



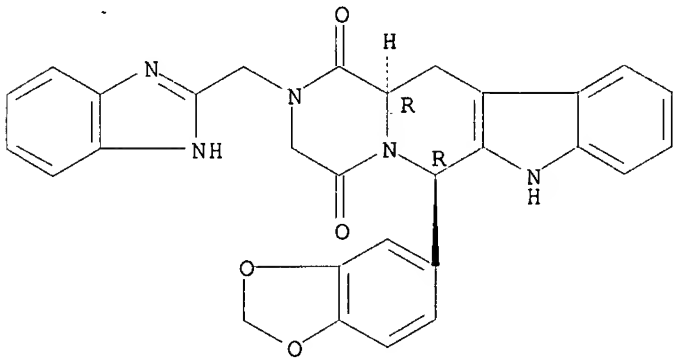
RN 385770-49-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[2-(3-azabicyclo[3.2.2]non-3-yl)ethyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



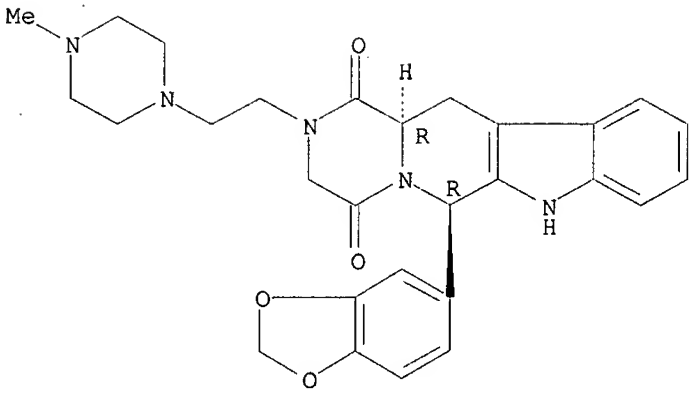
RN 385770-50-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-(1H-benzimidazol-2-ylmethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



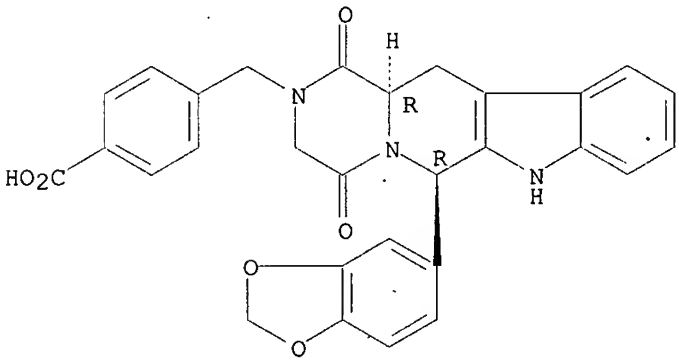
RN 385770-52-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(4-methyl-1-piperazinyl)ethyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



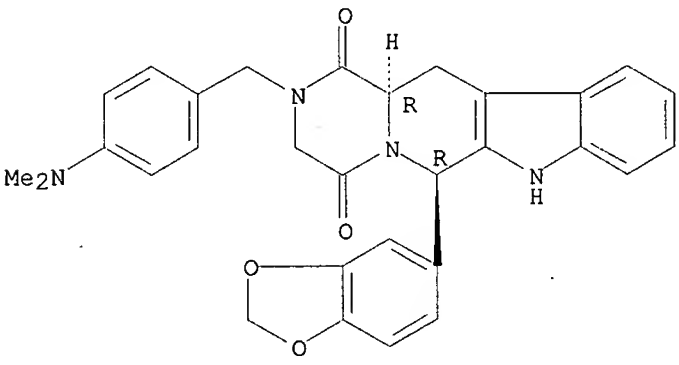
RN 385770-54-7 CAPLUS
CN Benzoic acid, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



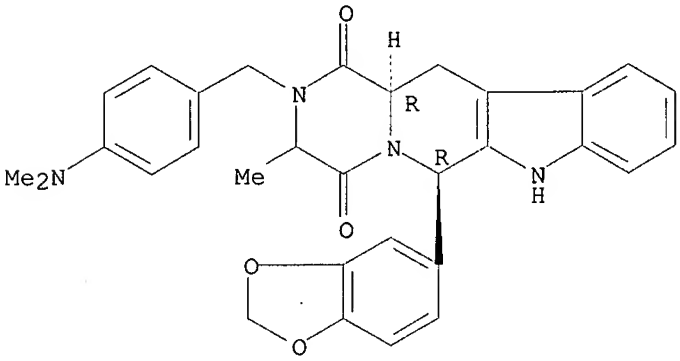
RN 385770-56-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-(dimethylamino)phenyl]methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



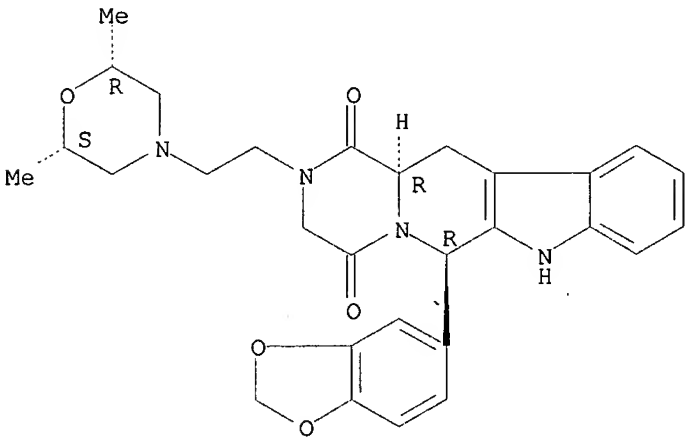
RN 385770-57-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-(dimethylamino)phenyl]methyl]-2,3,6,7,12,12a-hexahydro-3-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



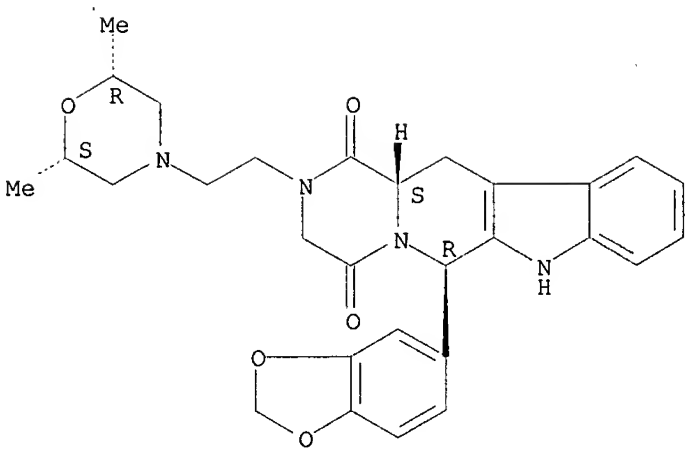
RN 385770-58-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethyl]-2,3,6,7,12,12a-hexahydro-, (6S,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



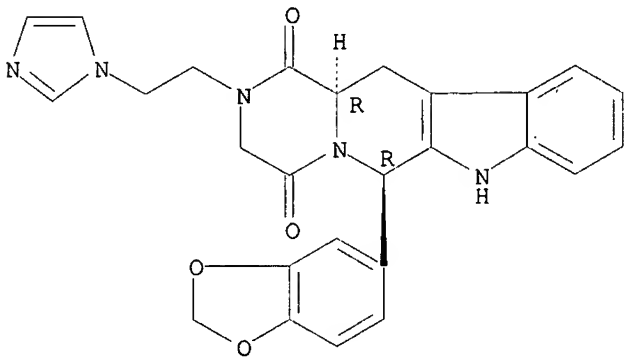
RN 385770-60-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethyl]-2,3,6,7,12,12a-hexahydro-, (6S,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



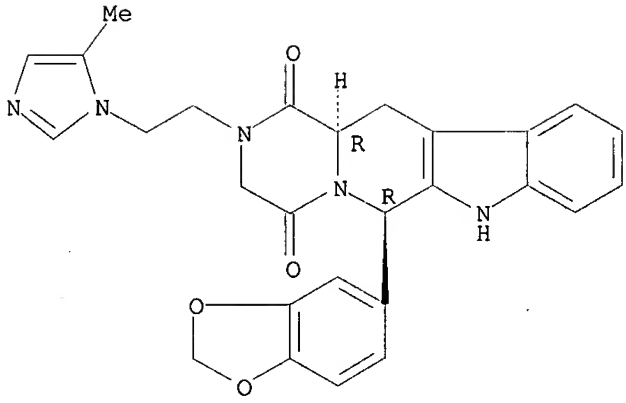
RN 385770-62-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-imidazol-1-yl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



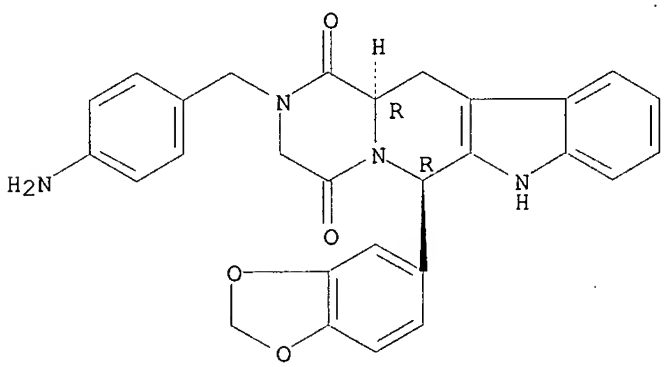
RN 385770-64-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(5-methyl-1H-imidazol-1-yl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



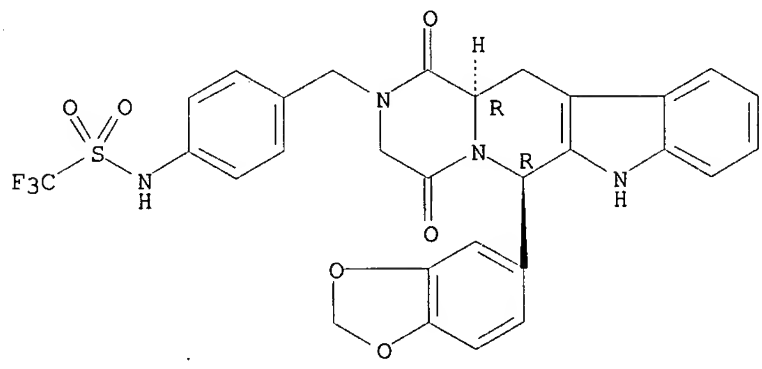
RN 385770-66-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[(4-aminophenyl)methyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



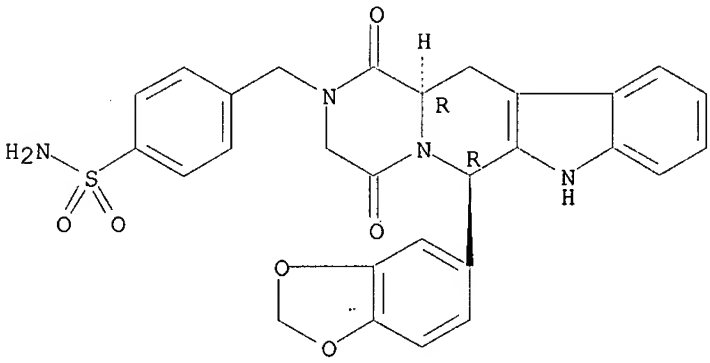
RN 385770-68-3 CAPLUS
CN Methanesulfonamide, N-[4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



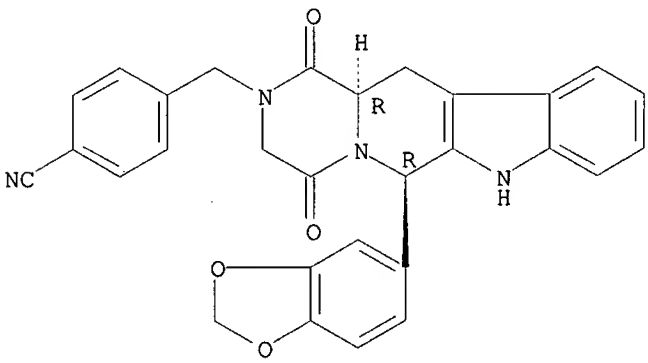
RN 385770-70-7 CAPLUS
CN Benzenesulfonamide, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



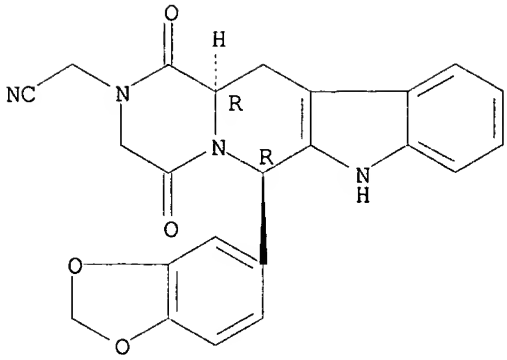
RN 385770-72-9 CAPLUS
CN Benzonitrile, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



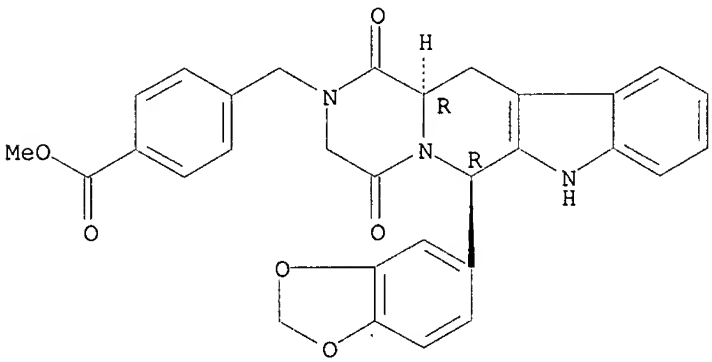
RN 385770-73-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetonitrile, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



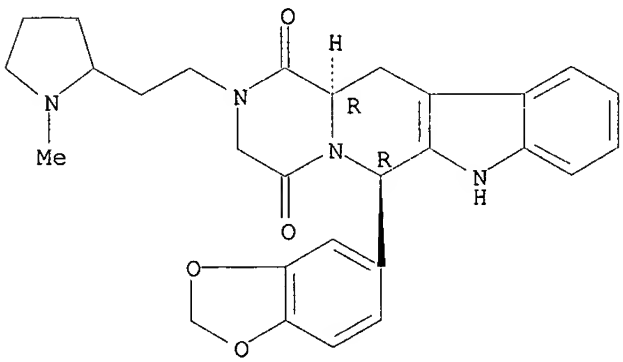
RN 385770-75-2 CAPLUS
CN Benzoic acid, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385770-76-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1-methyl-2-pyrrolidinyl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

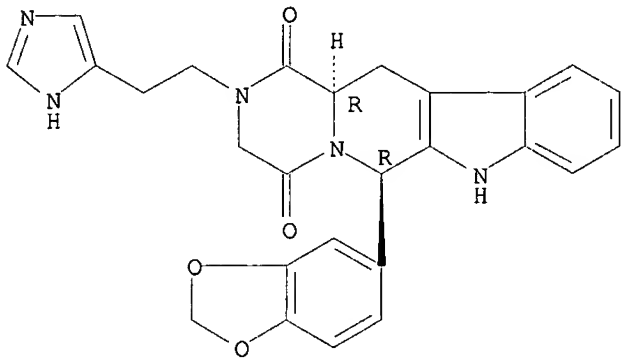
Relative stereochemistry.



RN 385770-77-4 CAPLUS

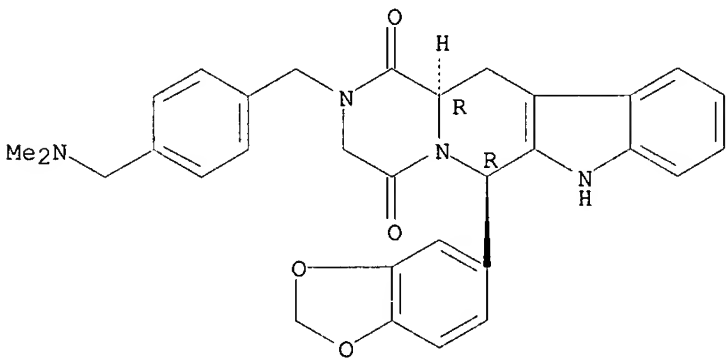
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-imidazol-4-yl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



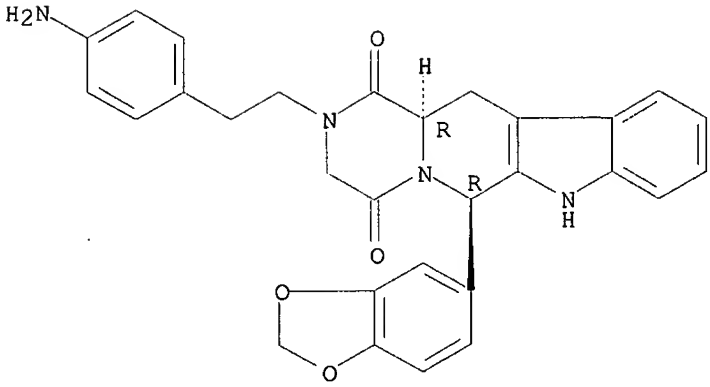
RN 385770-78-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-[(dimethylamino)methyl]phenyl]methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



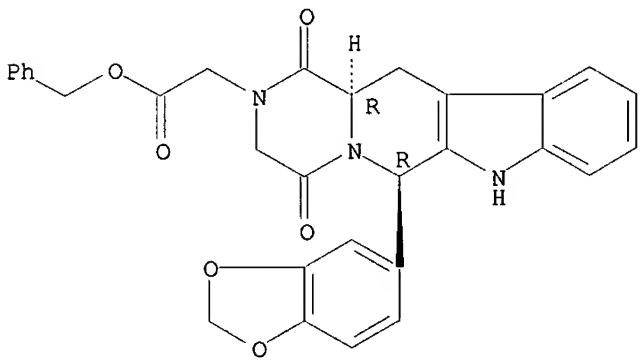
RN 385770-79-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[2-(4-aminophenyl)ethyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



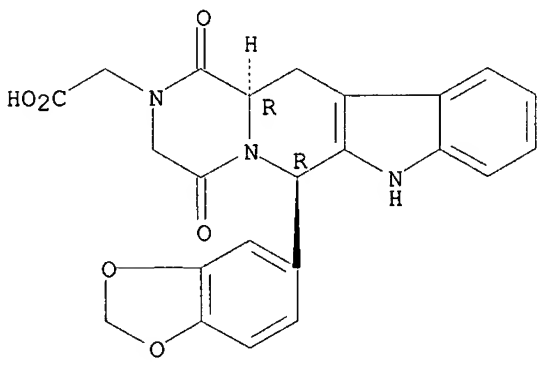
RN 385770-80-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, phenylmethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



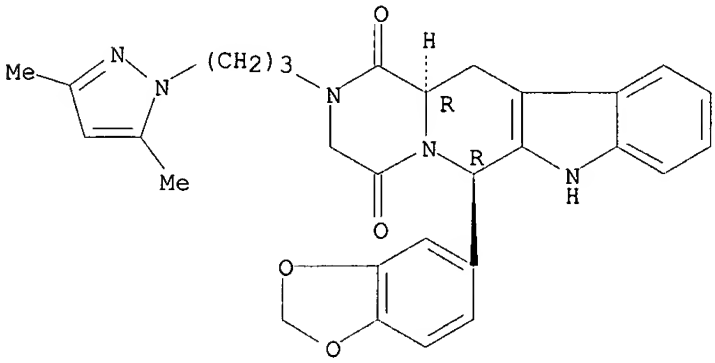
RN 385770-82-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



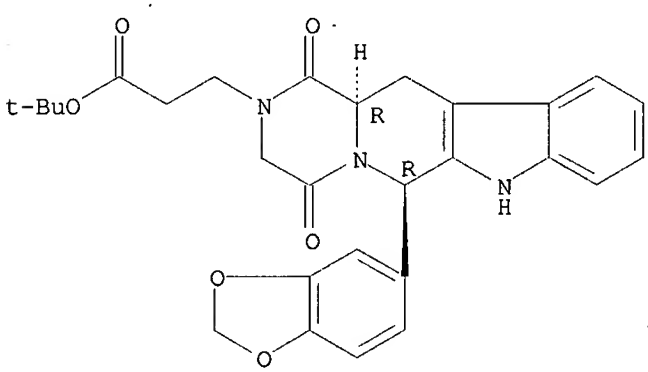
RN 385770-83-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[3-(3,5-dimethyl-1H-pyrazol-1-yl)propyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



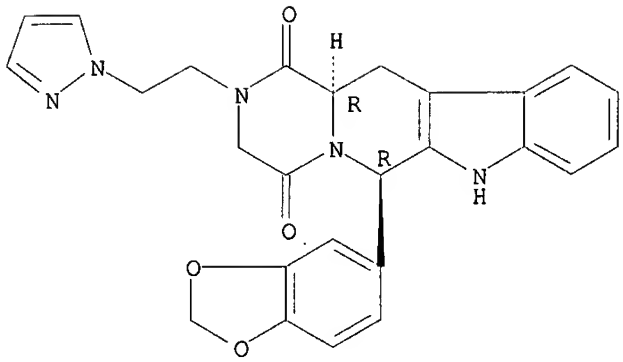
RN 385770-85-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanoic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



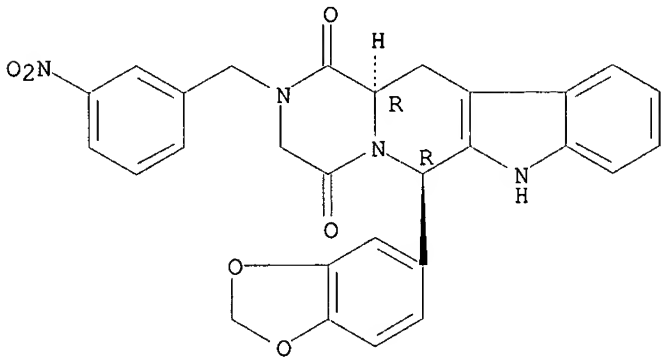
RN 385770-89-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-pyrazol-1-yl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



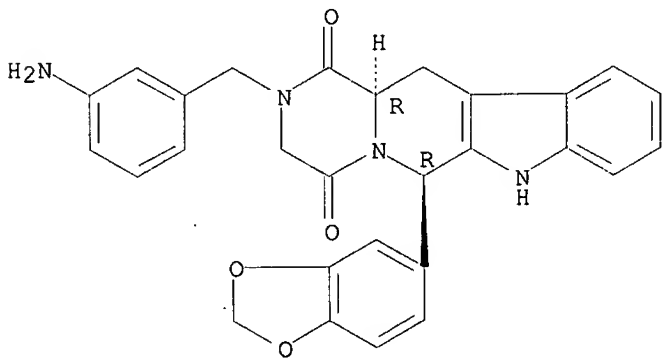
RN 385770-91-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3-nitrophenyl)methyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385770-92-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[(3-aminophenyl)methyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

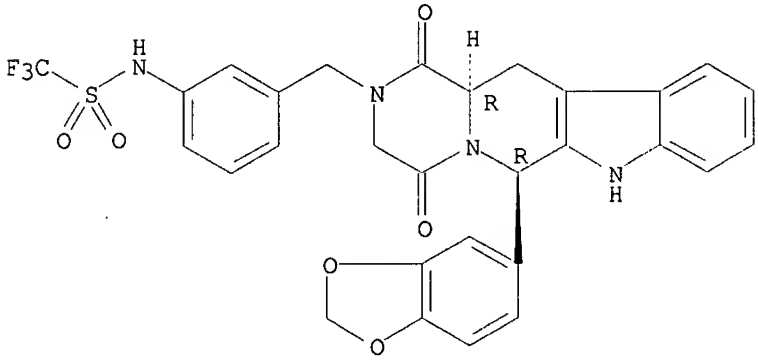
Absolute stereochemistry.



RN 385770-93-4 CAPLUS

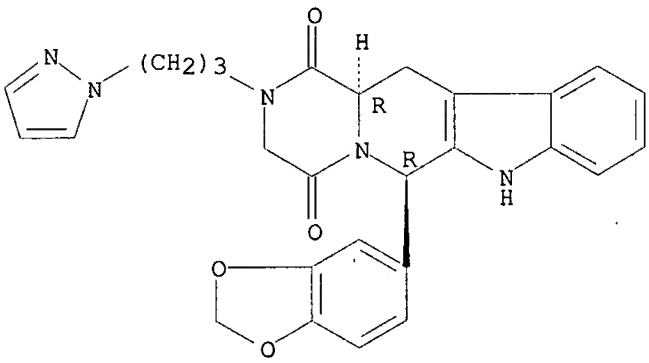
CN Methanesulfonamide, N-[3-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



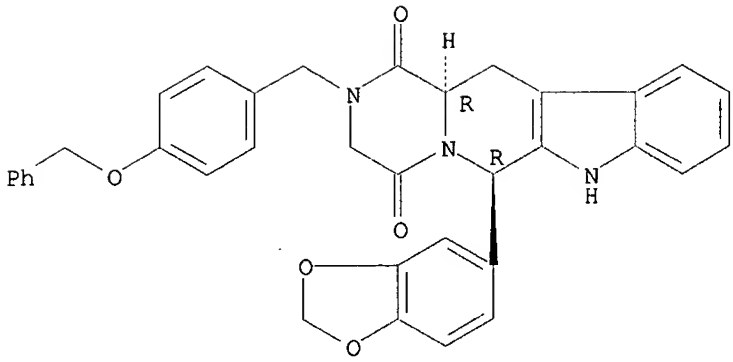
RN 385770-95-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(1H-pyrazol-1-yl)propyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



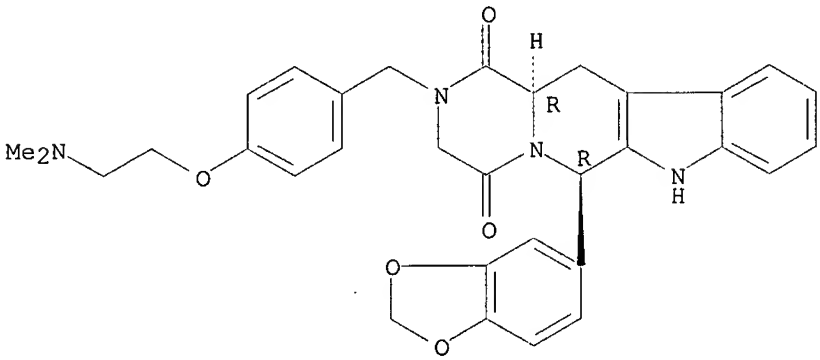
RN 385770-96-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[[4-(phenylmethoxy)phenyl]methyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



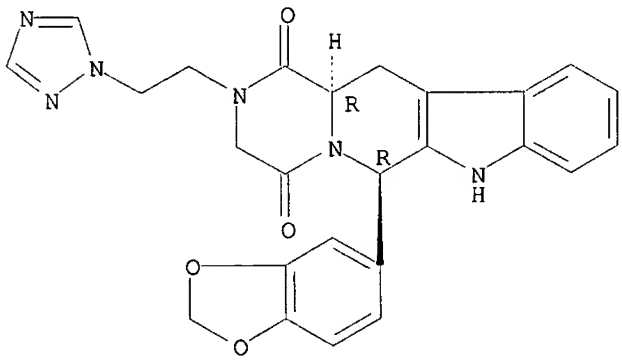
RN 385770-98-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-[2-(dimethylamino)ethoxy]phenyl]methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385770-99-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-1,2,4-triazol-1-yl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

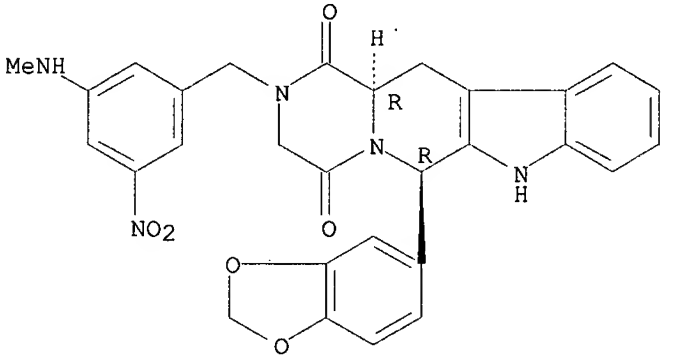
Absolute stereochemistry.



RN 385771-02-8 CAPLUS

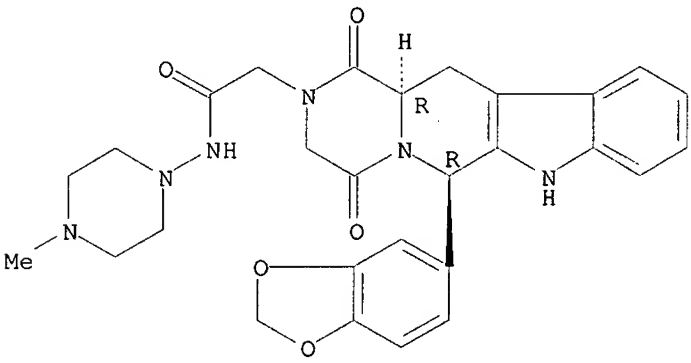
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[[3-(methylamino)-5-nitrophenyl]methyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



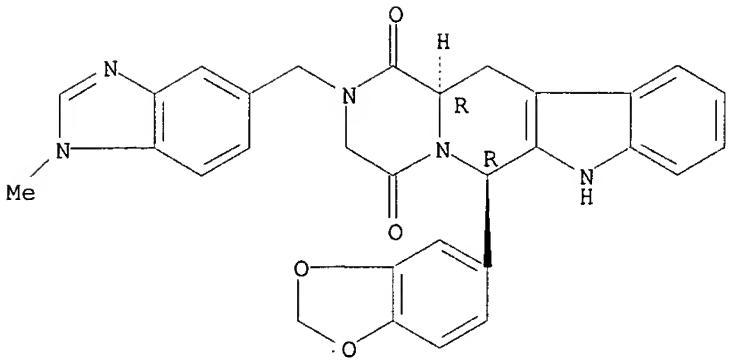

RN 385771-03-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-N-(4-methyl-1-piperazinyl)-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



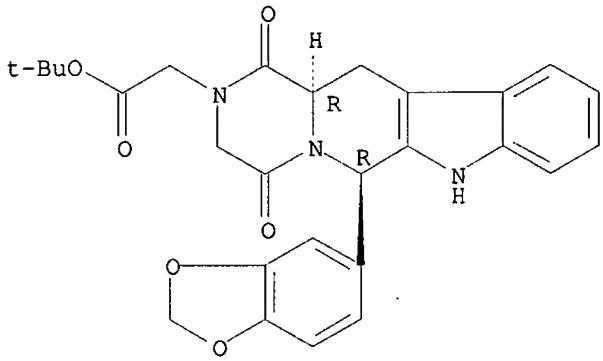

RN 385771-05-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(1-methyl-1H-benzimidazol-5-yl)methyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



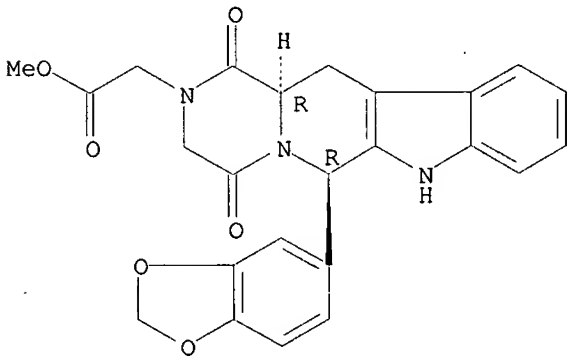
RN 385771-06-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385771-08-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, methyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

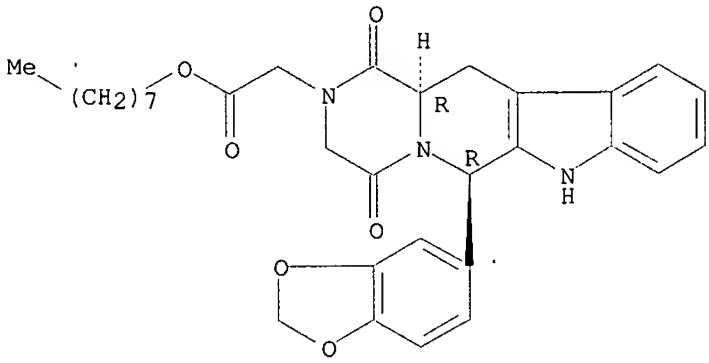
Absolute stereochemistry.



RN 385771-10-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, octyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:924320 CAPLUS
DOCUMENT NUMBER: 136:31728
TITLE: Daily treatment for erectile dysfunction using a phosphodiesterase 5 (PDE5) inhibitor
INVENTOR(S): Whitaker, John S.; Saenz de Tejada, Inigo; Ferguson, Kenneth M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 558,911.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2001053780 | A1 | 20011220 | US 2001-834442 | 20010413 |
| EP 1173181 | A2 | 20020123 | EP 2000-926367 | 20000426 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| NO 2001005275 | A | 20011206 | NO 2001-5275 | 20011029 |

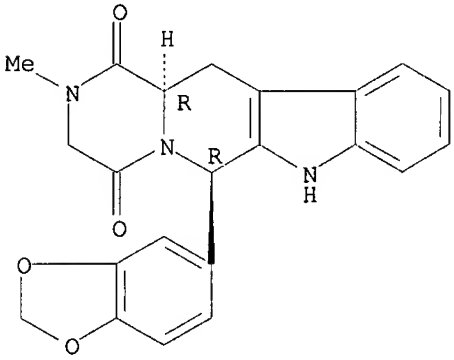
PRIORITY APPLN. INFO.:
US 1999-132036P P 19990430
US 2000-558911 A2 20000426
WO 2000-US11129 W 20000426

AB The invention provides phosphodiesterase (PDE) enzyme inhibitors and to their use in pharmaceutical articles of manuf. In particular, the invention provides potent inhibitors of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase type 5 (PDE5) that, when incorporated into a pharmaceutical product at about 1-10 mg unit dosage, are useful for the treatment of sexual dysfunction by daily administration of the PDE5 inhibitor. The articles of manuf. described are characterized by PDE5 inhibition, and accordingly, provide a benefit in therapeutic areas where inhibition of PDE5 is desired, esp. erectile dysfunction, with minimization or elimination of adverse side effects resulting from inhibition of other phosphodiesterase enzymes and with an improvement of vascular conditioning.

IT **171596-29-5 171596-40-0**

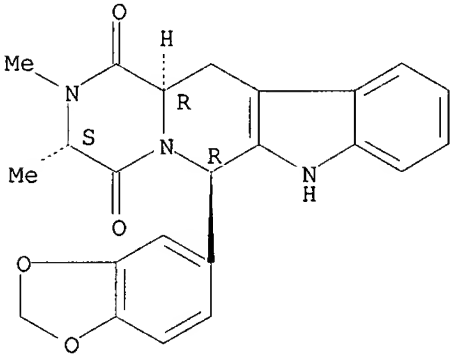
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 5 inhibitor for daily treatment for erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:916407 CAPLUS
DOCUMENT NUMBER: 136:53755
TITLE: Synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction
INVENTOR(S): Garvey, David S.; Saenz de Tejada, Inigo; Earl, Richard A.; Khanapure, Subhash P.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S., 117 pp., Cont.-in-part of U.S. 5,958,926.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6331543 | B1 | 20011218 | US 1999-387727 | 19990901 |
| US 5874437 | A | 19990223 | US 1996-740764 | 19961101 |
| WO 9819672 | A1 | 19980514 | WO 1997-US19870 | 19971031 |
| W: AU, CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5958926 | A | 19990928 | US 1998-145142 | 19980901 |
| US 2002019405 | A1 | 20020214 | US 2001-941691 | 20010830 |

PRIORITY APPLN. INFO.: US 1996-740764 A2 19961101
WO 1997-US19870 A2 19971031
US 1998-145142 A2 19980901
US 1999-387727 A1 19990901

OTHER SOURCE(S): MARPAT 136:53755
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

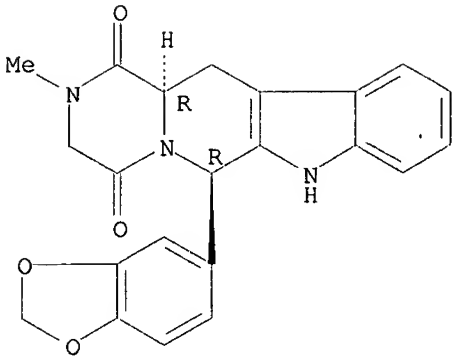
AB Compds. I-V, derivs. thereof, and certain substituted Ph and phthalzaine derivs. were claimed [D2 = H, alkyl, D; D = NO, NO2, alkyl, acyl, phosphoryl, silyl, etc.; A1-3 comprise the other subunits of a 5- or 6-membered monocyclic arom. ring; R8 = H, (halo)alkyl; p = 1-10; R24 = H, cyclohexyl, piperidinyl, etc., with the proviso that at least one of A1-3, J, or R24 contains T-Q or D; T = bond, O, S(O), amino; Q = NO, NO2; D1 = D or H; R37 = (hetero)aryl; R38 = H, halo, alkyl; G1 = alkyl, alkenyl or is part of a ring fused to the piperidine moiety of III; G4 = O, S; R40 = H, alkyl, haloalkyl, halo, etc.; R41 = alkyl, hydroxyalkyl, alkylcarboxy, etc.; R42 = aryl, alkylaryl, alkyloxyaryl; T1 = alkyl, oxyalkyl, thioalkyl, aminoalkyl]. Two synthetic examples were provided. E.g., the S-nitroso deriv. of the 3-mercapto-3-methylbutyric acid ester of dipyridamole (VI) was prepd. in 4 steps from dipyridamole in 3.5% overall yield. VI at doses of 10 and 30 .mu.M was more efficacious in relaxing phenylephrine-induced tissue contraction than was the known phosphodiesterase inhibitor, dipyridamole. The present invention describes novel (nitrosated/nitrosylated) phosphodiesterase inhibitors, and compns. contg. at least one (nitrosated/nitrosylated) phosphodiesterase inhibitor, and, optionally, one or more compds. that donate, transfer or release NO, elevate endogenous levels of endothelium-derived relaxing factor, stimulate endogenous synthesis of NO, or is a substrate for nitric oxide synthase and/or one or more vasoactive agents. The present invention also provides methods for treating or preventing sexual dysfunctions in males and females, for enhancing sexual responses in males and females, and for treating or preventing diseases induced by the increased metab. of cGMP, such as hypertension, pulmonary hypertension, etc.

IT **171596-29-5D**, ICOS 351, nitroso derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



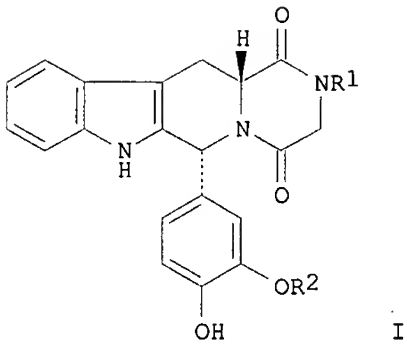
REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:904172 CAPLUS
DOCUMENT NUMBER: 136:20091
TITLE: Preparation of tetracyclic diketopiperazine compounds as PDE5 inhibitor
INVENTOR(S): Orme, Mark W.; Daugan, Alain Claude-Marie; Bombrun, Agnes
PATENT ASSIGNEE(S): Lilly Icos Llc, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001094347 | A1 | 20011213 | WO 2001-US15937 | 20010515 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-210324P P 20000608
OTHER SOURCE(S): MARPAT 136:20091
GI



I

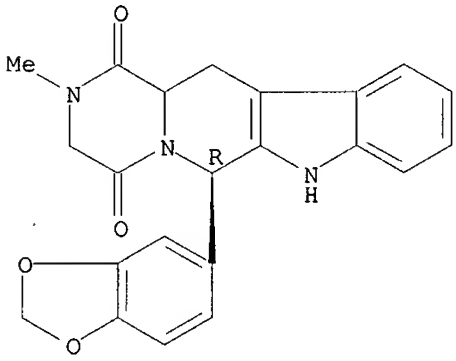
AB The title compds. I [R1 = C1-6 alkyl; R2 = H, Me] were prepd. and use of the compds. as PDE5 inhibitors was described.. E.g., (6R,12aR)-6-(3,4-dihydroxyphenyl)-2-methyl-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione was prepd. I may be used for male erectile dysfunction or female arousal disorder.

IT **378788-17-1P**
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of tetracyclic diketopiperazine compds. as PDE5 inhibitor)

RN 378788-17-1 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:904168 CAPLUS

DOCUMENT NUMBER: 136:20090

TITLE: Preparation of cyclic guanosine monophosphate specific phosphodiesterase inhibiting heterocyclylpyrazinopyridoindolediones for treatment of cardiovascular disorders and erectile disfunction

INVENTOR(S): Orme, Mark W.; Sawyer, Jason Scott; Daugan, Alain Claud-Marie

PATENT ASSIGNEE(S): Lilly Icos LLC, USA

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001094345 | A2 | 20011213 | WO 2001-US15936 | 20010515 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-210137P P 20000607
OTHER SOURCE(S): MARPAT 136:20090
GI

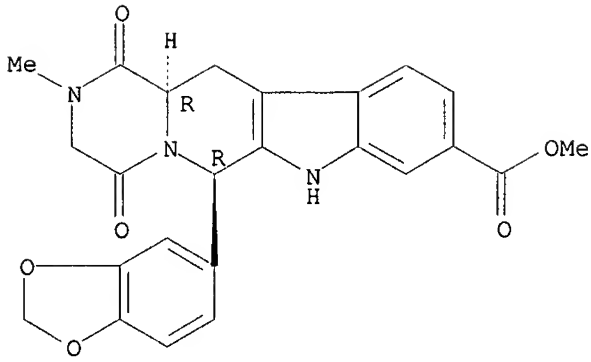
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The pyrazinopyridoindolediones I [R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, heterocycloalkyl, etc; R2 = (un)substituted Ph, thienyl, furanyl, pyridyl, bicyclic ring optionally contg. O, S, N hetero atoms, e.g. benzodioxolyl; R3 = H, alkyl; R4 = aryl, heteroaryl, cycloalkyl, acyl, acyloxy, alkoxycarbonyl, aminoalkyl, carbamoyl, alkoxy, amino, acylamino, nitro, cyano, alkylthio etc.; R5 = H, halo, alkyl; R4R5 = 5-, 6-, 7-membered ring optionally contg. O, S, N atoms; m = 1, 2, 3 ] and their diastereoisomers and pharmaceutically acceptable salts were prepd., possessed cGMP specific phosphodiesterase inhibiting activity, and were useful in the treatment of various cardiovascular disorders, erectile disfunction, and female sexual arousal disorder. Thus, the Me ester of 5-hydroxytryptophan condensed with piperonal in trifluoroacetic acid/CH2Cl2 to give the [(methylenedioxy)phenyl]pyridoindole II which was acylated by ClCH2COCl and then cyclized with MeNH2 to give the [(methylenedioxy)phenyl]hexahydropyrazinopyridoindoledione III that inhibited cGMP specific phosphodiesterase in vitro with an IC50 of 48.1 nM.

IT **379234-97-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of (benzodioxolyl)pyrazinopyridoindolediones with cGMP-specific phosphodiesterase inhibiting activity useful in treating cardiovascular, erectile, and female sexual arousal disorders)

RN 379234-97-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-9-carboxylic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, methyl ester, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

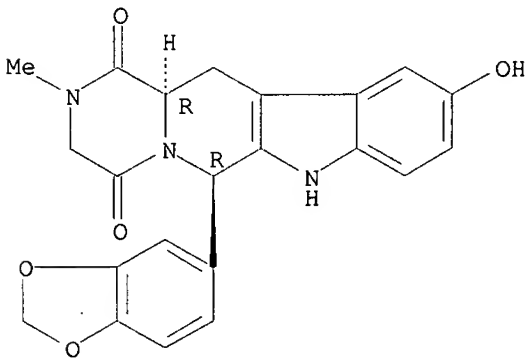
Relative stereochemistry.



IT **379234-74-9P 379234-78-3P 379234-82-9P**
**379234-88-5P 379234-98-7P 379235-06-0P**
**379235-11-7P 379235-12-8P 379235-13-9P**
**379235-14-0P 379235-15-1P 379235-16-2P**
**379235-17-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (benzodioxolyl)pyrazinopyridoindolediones with cGMP-specific phosphodiesterase inhibiting activity useful in treating cardiovascular, erectile, and female sexual arousal disorders)

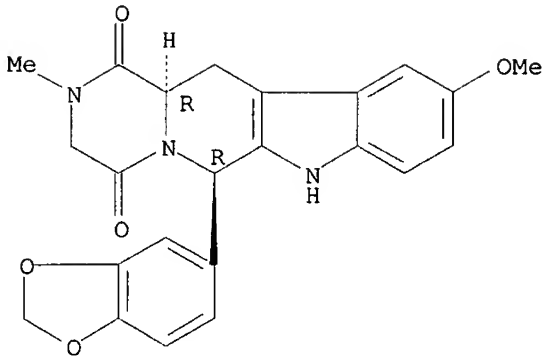
RN 379234-74-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-10-hydroxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



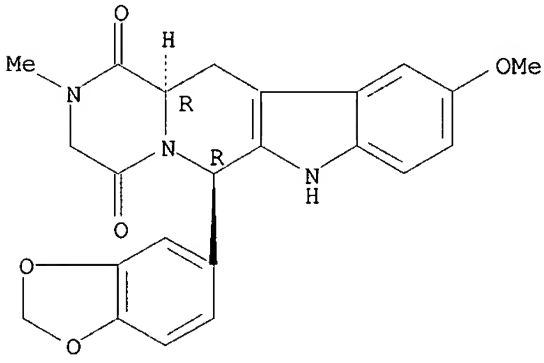
RN 379234-78-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-10-methoxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



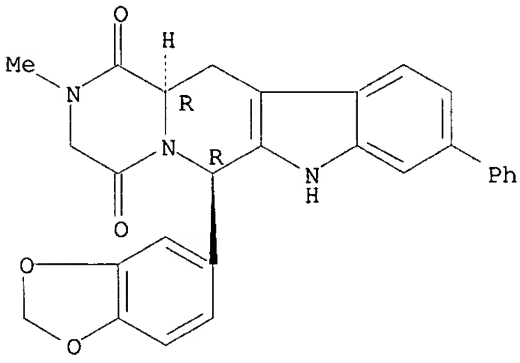
RN 379234-82-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-10-methoxy-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 379234-88-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-9-phenyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

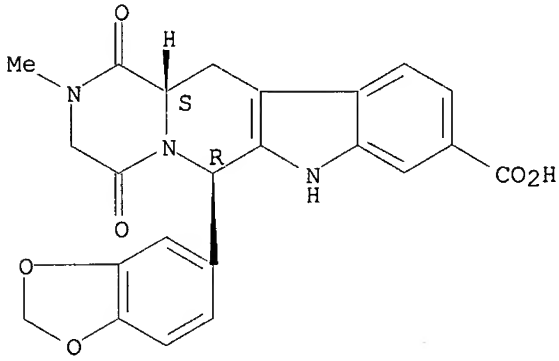
Relative stereochemistry.



RN 379234-98-7 CAPLUS

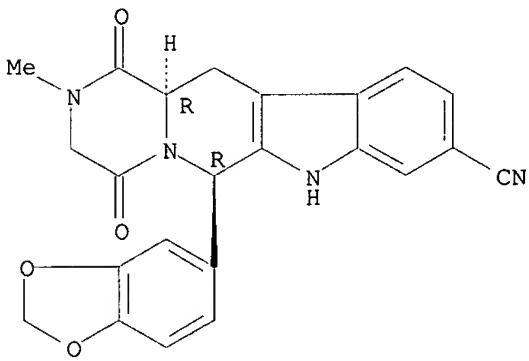
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-9-carboxylic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



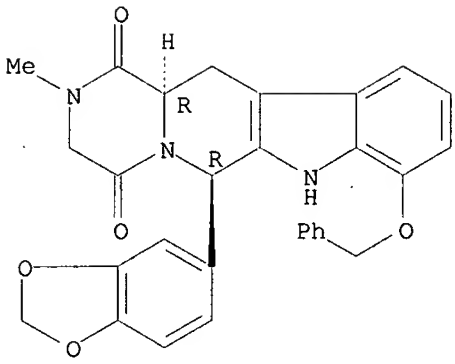
RN 379235-06-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-9-carbonitrile, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



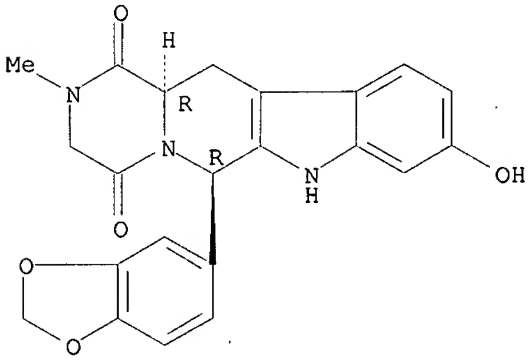
RN 379235-11-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-8-(phenylmethoxy)-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



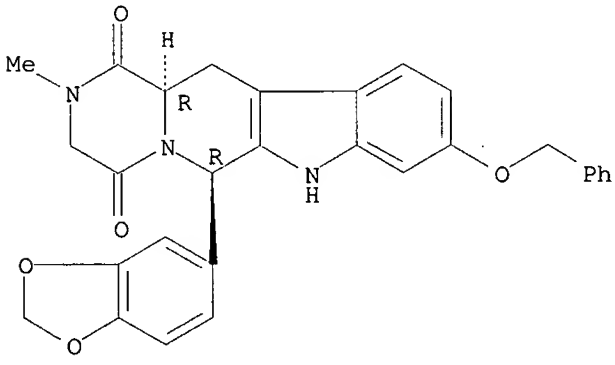
RN 379235-12-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-9-hydroxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 379235-13-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-9-(phenylmethoxy)-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

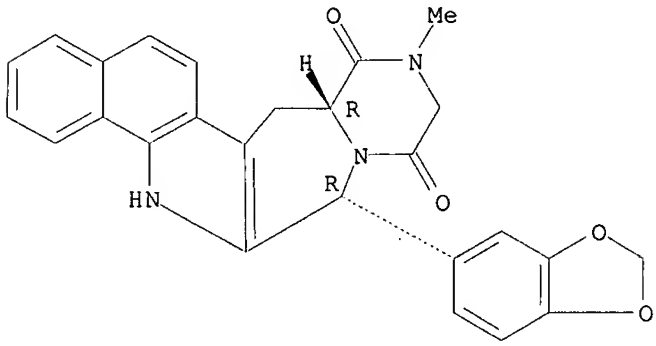
Relative stereochemistry.



RN 379235-14-0 CAPLUS

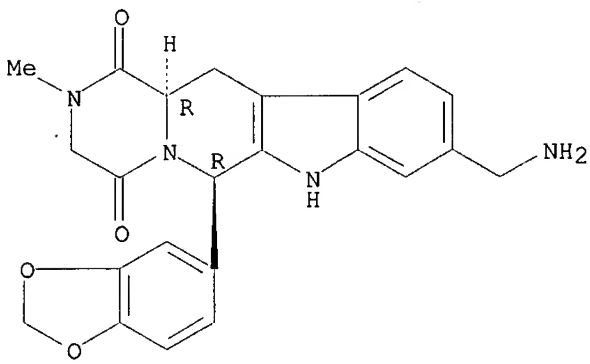
CN Benzo[g]pyrazino[1',2':1,6]pyrido[3,4-b]indole-8,11-dione, 13-(1,3-benzodioxol-5-yl)-7,7a,9,10,13,14-hexahydro-9-methyl-, (7aR,13R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



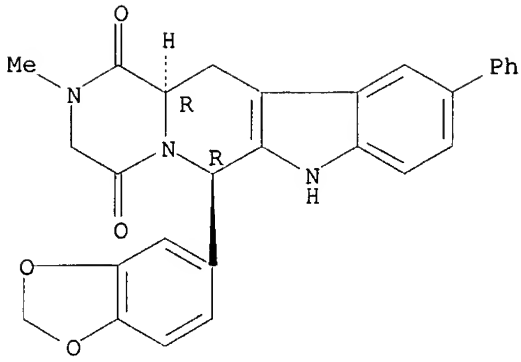

RN 379235-15-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 9-(aminomethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



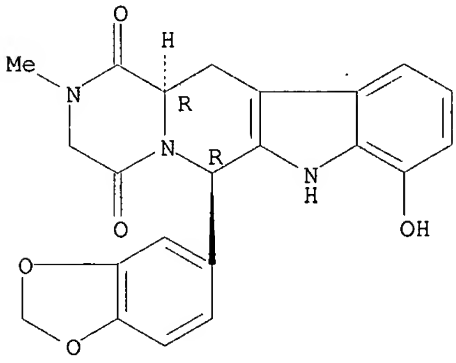

RN 379235-16-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-10-phenyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



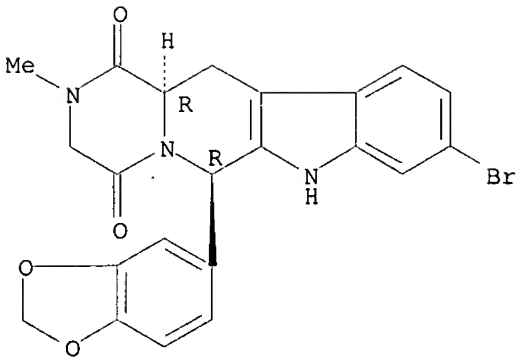
RN 379235-17-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-8-hydroxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **379234-87-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (benzodioxolyl)pyrazinopyridoindolediones with cGMP-specific phosphodiesterase inhibiting activity useful in treating cardiovascular, erectile, and female sexual arousal disorders)
RN 379234-87-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-9-bromo-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L12 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798055 CAPLUS
DOCUMENT NUMBER: 135:339295
TITLE: Daily treatment for erectile dysfunction using a phosphodiesterase 5 (PDE5) inhibitor
INVENTOR(S): Whitaker, John S.; Saenz de Tejada, Inigo; Ferguson, Kenneth M.
PATENT ASSIGNEE(S): Lilly Icos LLC, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001080860 | A2 | 20011101 | WO 2001-US12512 | 20010413 |
| WO 2001080860 | A3 | 20020606 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-558911 A 20000426

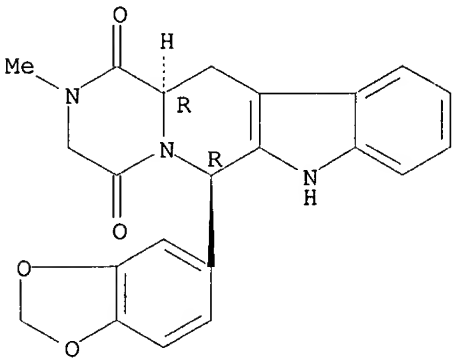
AB The invention relates to phosphodiesterase (PDE) enzyme inhibitors and to their use in pharmaceutical articles of manuf. In particular, the invention relates to potent inhibitors of cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase type 5 (PDE5) that, when incorporated into a pharmaceutical product at about 1 to about 10 mg unit dosage, are useful for the treatment of sexual dysfunction by daily administration of the PDE5 inhibitor. The articles of manuf. are characterized by PDE5 inhibition, and accordingly provide a benefit in therapeutic areas where inhibition of PDE5 is desired, esp. erectile dysfunction, with minimization or elimination of adverse side effects resulting from inhibition of other phosphodiesterase enzymes and with an improvement of vascular conditioning.

IT **171596-29-5 171596-40-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(phosphodiesterase 5 inhibitor for daily treatment for sexual dysfunction)

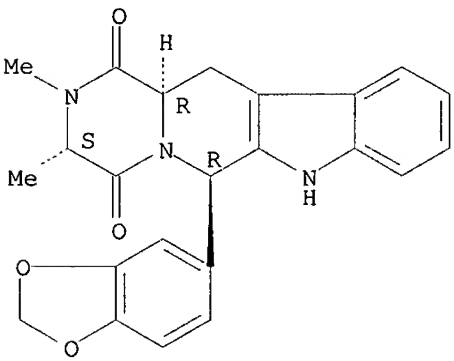
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:713326 CAPLUS
DOCUMENT NUMBER: 135:272990
TITLE: Preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as melanocortin-4 receptor agonists
INVENTOR(S): Palucki, Brenda L.; Barakat, Khaled J.; Guo, Liangqin; Lai, Yingjie; Nargund, Ravi P.; Park, Min K.; Pollard, Patrick G.; Sebhat, Iyassu K.; Ye, Zhixiong
PATENT ASSIGNEE(S): Merck + Co., Inc., USA
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001070708 | A1 | 20010927 | WO 2001-US8935 | 20010320 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

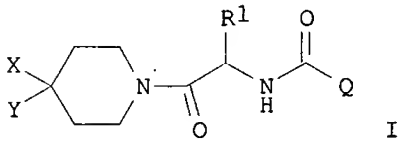
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 2002019523 | A1 | 20020214 | US 2001-812965 | 20010320 |

PRIORITY APPLN. INFO.:
US 2000-191442P P 20000323
US 2000-242265P P 20001020

OTHER SOURCE(S): MARPAT 135:272990

GI



I

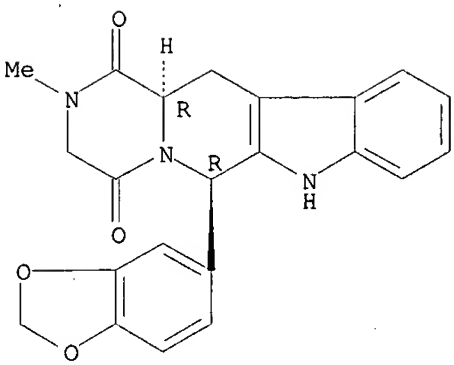
AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepd. as melanocortin-4 receptor (MC-4R) agonists. Thus, capsule formulations contg. title compd. (II) were prepd. Representative I activated MC-4R with IC50<1 .mu.M. I are claimed for the treatment of obesity, diabetes, and sexual dysfunction including erectile dysfunction and female sexual dysfunction.

IT **171596-29-5**, IC-351
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as melanocortin-4 receptor agonists)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:559496 CAPLUS
DOCUMENT NUMBER: 135:117266
TITLE: Treatment of sexual function disorders with phosphodiesterase 4 inhibitors as monotherapy or in combination with other phosphodiesterase inhibitors or adenylate cyclase activators
PATENT ASSIGNEE(S): Stief, Christian, Germany
SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

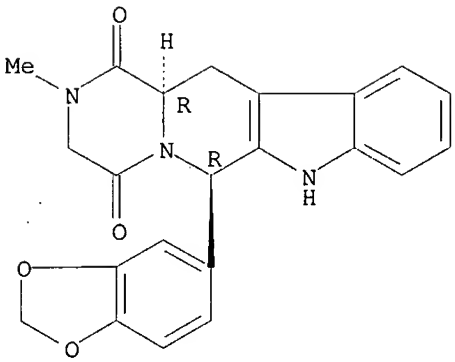
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10004289 | A1 | 20010802 | DE 2000-10004289 | 20000201 |

AB The invention provides a medicament contg. a phosphodiesterase 4 inhibitor as monotherapy or in combination with other phosphodiesterase inhibitors or adenylate cyclase activators for the treatment of s sexual function disorders.

IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 inhibitors as monotherapy or in combination with other phosphodiesterase inhibitors or adenylate cyclase activators for treatment of sexual function disorders)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:541505 CAPLUS
DOCUMENT NUMBER: 135:132460
TITLE: Treatment of sexual function disorders with guanylate cyclase activators, optionally in combination with phosphodiesterase inhibitors
INVENTOR(S): Stief, Christian; Magerl, Hans-Jurgen; Kuthe, Andrea; Uckert, Stefan; Becker, Armin; Farssmann, Wolf Georg; Jones, Udo
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

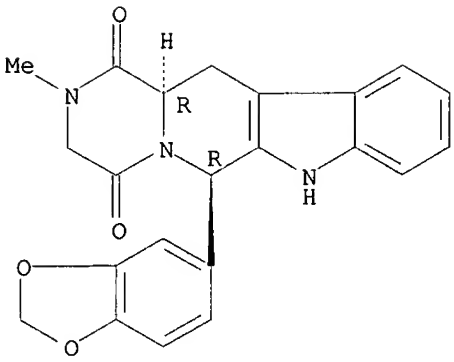
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 10002200 | A1 | 20010726 | DE 2000-10002200 | 20000119 |

AB Medicaments contg. activators of guanylate cyclase and their variants, individually or in combination with phosphodiesterase inhibitors, are provided for the treatment of sexual function disorders. e.g. erectile dysfunction.

IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(guanylate cyclase activators, optionally in combination with phosphodiesterase inhibitors, for treatment of sexual function disorders)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:338071 CAPLUS
DOCUMENT NUMBER: 134:336223
TITLE: Treatment of pulmonary hypertension with sildenafil or other phosphodiesterase V inhibitor
INVENTOR(S): Butrous, Ghazwan Saleem; Lukas, Timothy; Machin, Ian
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1097711 | A2 | 20010509 | EP 2000-309212 | 20001101 |
| EP 1097711 | A3 | 20010801 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2001172182 | A2 | 20010626 | JP 2000-335765 | 20001102 |

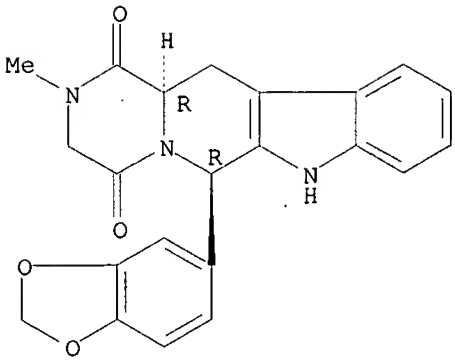
PRIORITY APPLN. INFO.: GB 1999-25970 A 19991102
GB 2000-3235 A 20000211

AB This invention relates to the use of certain cyclic guanosine 3',5'-monophosphate phosphodiesterase type 5 inhibitors, including in particular the compd. sildenafil, for the treatment of pulmonary hypertension.

IT **171596-29-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sildenafil or other phosphodiesterase V inhibitor for treatment of pulmonary hypertension)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



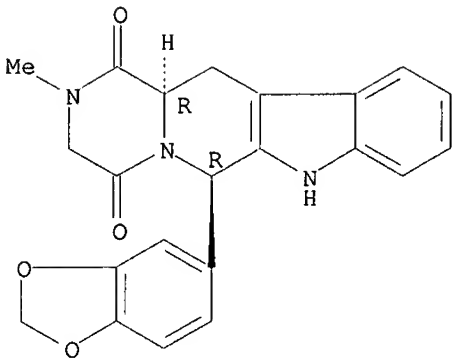
L12 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:258390 CAPLUS
DOCUMENT NUMBER: 135:189567
TITLE: IC-351: Treatment of erectile dysfunction treatment of female sexual dysfunction phosphodiesterase 5 inhibitor
AUTHOR(S): Sorbera, L. A.; Martin, L.; Leeson, P. A.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2001), 26(1), 15-19
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 20 refs. Significantly more patients (86 %) given IC-351 reported enhanced erections as compared to placebo and a significant change in the patient's median rating was obsd. with IC-351 treatment as compared to placebo. IC-351 (ClalisTM) continues to undergo phase III trials as a treatment for male erectile dysfunction and phase II trials as a treatment for female sexual dysfunction.

IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IC-351 in treatment of erectile dysfunction and treatment of female sexual dysfunction in humans)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:100983 CAPLUS
DOCUMENT NUMBER: 134:152655
TITLE: Pharmaceutical compositions containing .beta.-carboline drugs
INVENTOR(S): Anderson, Neil R.; Hartauer, Kerry J.; Kral, Martha A.; Stephenson, Gregory A.
PATENT ASSIGNEE(S): Lilly Icos Llc, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001008688 | A2 | 20010208 | WO 2000-US20981 | 20000801 |
| WO 2001008688 | A3 | 20010816 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000012901 | A | 20020416 | BR 2000-12901 | 20000801 |
| EP 1200092 | A2 | 20020502 | EP 2000-952371 | 20000801 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| NO 2002000531 | A | 20020403 | NO 2002-531 | 20020201 |

PRIORITY APPLN. INFO.: US 1999-147048P P 19990803
WO 2000-US20981 W 20000801

AB Pharmaceutical compns. contg. .beta.-carboline drugs and pharmaceutically acceptable salts and solvates thereof, wherein the drug is in free particulate form, is disclosed. A tablet contained a .beta.-carboline drug 10.00, lactose monohydrate 153.80, spray dried lactose monohydrate 25.00, hydroxypropyl cellulose 4.00, croscarmellose sodium 16.00, hydroxypropyl cellulose 1.75, sodium lauryl sulfate 0.70, microcryst. cellulose 37.50, and magnesium stearate 1.25 mg. The improvement in

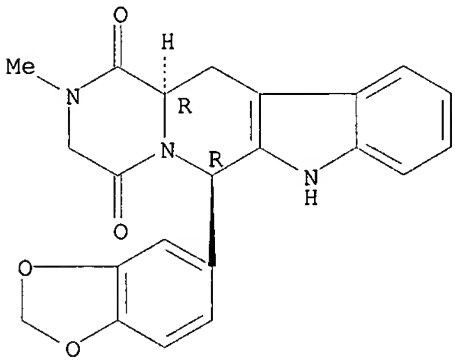
bioavailability of the drug was demonstrated in humans.

IT **171596-29-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. .beta.-carboline drugs)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:100982 CAPLUS
DOCUMENT NUMBER: 134:152654
TITLE: .beta.-Carboline pharmaceutical compositions
INVENTOR(S): Anderson, Neil R.; Gullapalli, Rampurna P.
PATENT ASSIGNEE(S): Lilly Icos Llc, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001008687 | A1 | 20010208 | WO 2000-US11136 | 20000426 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1200091 | A1 | 20020502 | EP 2000-926371 | 20000426 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |

PRIORITY APPLN. INFO.: US 1999-146924P P 19990803
WO 2000-US11136 W 20000426

AB .beta.-Carboline soft capsules contains a soln. or suspension of a PDE5 inhibitor, and are useful for treating sexual dysfunction. Thus, a formulation contained a .beta.-carboline 25.0, Capmul MCM 177.5, Gelucire 44/14 177.5, and propylene glycol 20.0 mg/capsule. In the phys. study of the above capsule formulation, no sedimentation was obsd. after storage at

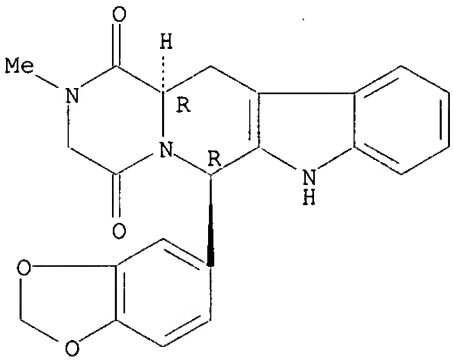
4.degree. for 120 days.

IT **171596-29-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-carboline pharmaceutical compns.)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:100981 CAPLUS
DOCUMENT NUMBER: 134:152653
TITLE: .beta.-Carboline pharmaceutical compositions containing cellulose
INVENTOR(S): Oren, Peter L.; Anderson, Neil R.; Kral, Martha A.
PATENT ASSIGNEE(S): Lilly Icos Llc, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001008686 | A1 | 20010208 | WO 2000-US11130 | 20000426 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000012863 | A | 20020416 | BR 2000-12863 | 20000426 |
| EP 1200090 | A1 | 20020502 | EP 2000-926368 | 20000426 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| NO 2002000532 | A | 20020326 | NO 2002-532 | 20020201 |

PRIORITY APPLN. INFO.: US 1999-146924P P 19990803
WO 2000-US11130 W 20000426

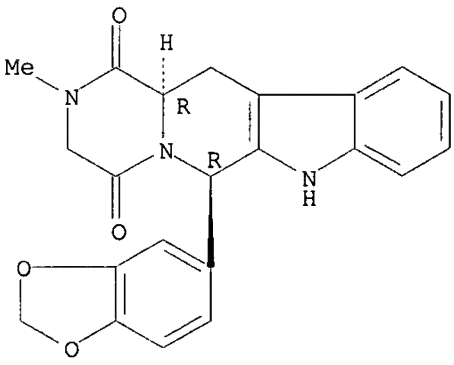
AB .beta.-Carboline formulations contain a c-GMP phosphodiesterase inhibitor, a water-sol. diluent, a lubricant, a hydrophilic binder, a disintegrant, and optional microcryst. cellulose and/or a wetting agent, are useful for treating sexual dysfunction. Thus, a tablet formulation contained a .beta.-carboline 5.00, lactose monohydrate 109.655, lactose monohydrate (spray dried) 17.50, Hydroxypropyl cellulose 4.025, croscarmellose sodium 6.30, SLS 0.49, microcryst. cellulose (granular-102) 26.25, croscarmellose sodium 4.90, and Mg stearate 0.88 mg/tablet.

IT **171596-29-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-carboline pharmaceutical compns. contg. cellulose)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:28490 CAPLUS
DOCUMENT NUMBER: 134:95523
TITLE: Drugs for the increase of the cAMP levels
INVENTOR(S): Stief, Christian G.; Ueckert, Stefan; Becker, Armin; Jonas, Udo; Forssmann, Wolf-Georg
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 6 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

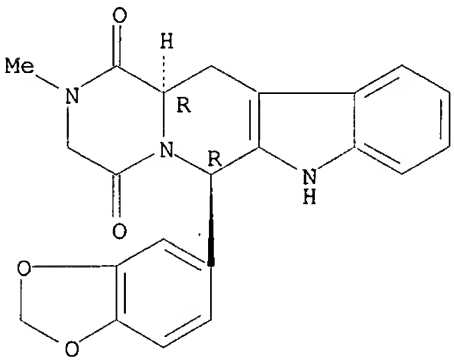
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 19931206 | A1 | 20010111 | DE 1999-19931206 | 19990707 |

AB The invention concerns drugs for the increase of the cAMP levels and/or for the inhibition of the cAMP hydrolysis in smooth muscle tissues and their use for the treatment of diseases. Compds. such as sildenafil increased the cAMP levels in smooth muscle tissues.

IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drugs for increase of cAMP levels)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




L12 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:790302 CAPLUS
DOCUMENT NUMBER: 133:329631
TITLE: Treatment of female arousal disorder with a type V cGMP phosphodiesterase inhibitor
INVENTOR(S): Allemeier, Lora L.; Brashear, Diane L.; Ferguson, Kenneth M.; Pullman, William E.
PATENT ASSIGNEE(S): Lilly Icos LLC, USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000066114 | A1 | 20001109 | WO 2000-US11128 | 20000426 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1173167 | A1 | 20020123 | EP 2000-928382 | 20000426 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |

PRIORITY APPLN. INFO.: US 1999-132129P P 19990430
WO 2000-US11128 W 20000426

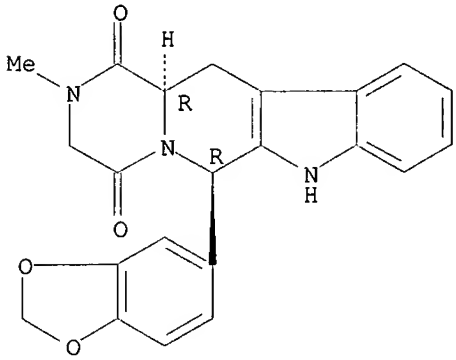
AB A method of treating female arousal disorder in a female patient is disclosed. The method includes orally administering an agent that inhibits cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase type 5 to the female patient.

IT **171596-29-5 171596-40-0 304683-09-8 304683-11-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cGMP phosphodiesterase type V inhibitor for treatment of female arousal disorder)

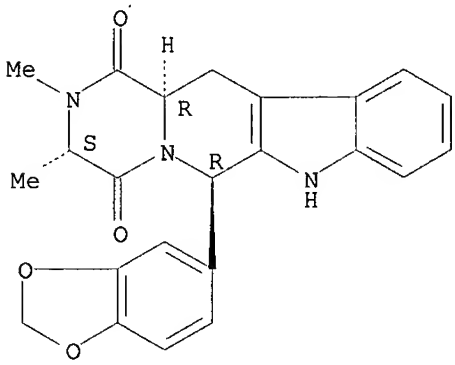
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

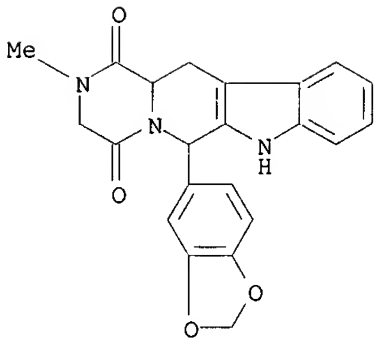


RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

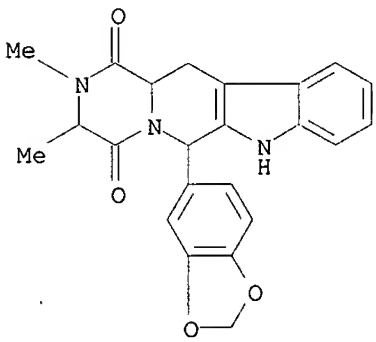
Absolute stereochemistry. Rotation (+).



RN 304683-09-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



RN 304683-11-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:785898 CAPLUS
DOCUMENT NUMBER: 133:329627
TITLE: Tetracyclic cGMP-specific phosphodiesterase inhibitors and their use in disease treatment
INVENTOR(S): Daugan, Alain Claude Marie; Gellibert, Francoise
PATENT ASSIGNEE(S): Icos Corp., USA
SOURCE: U.S., 30 pp., Cont.-in-part of PCT 9519978.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6143746 | A | 20001107 | US 1998-154051 | 19980916 |
| WO 9519978 | A1 | 19950727 | WO 1995-EP183 | 19950119 |

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US

RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
WO 9703675 A1 19970206 WO 1996-EP3024 19960711
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
WO 9703985 A1 19970206 WO 1996-EP3025 19960711
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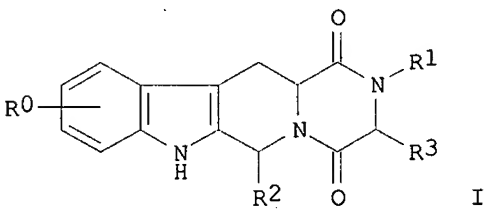
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
US 6025494 A 20000215 US 1998-133078 19980812
EP 1113800 A1 20010711 EP 1999-945201 19990826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
US 6127542 A 20001003 US 1999-399667 19990921
PRIORITY APPLN. INFO.: GB 1994-1090 A 19940121
WO 1995-EP183 A2 19950119
GB 1995-14464 A 19950714
GB 1995-14465 A 19950714
WO 1996-EP3024 A2 19960711
WO 1996-EP3025 A2 19960711
US 1996-669389 A3 19960716
US 1998-133078 A1 19980812
US 1998-154051 A 19980916
WO 1999-US19466 W 19990826
OTHER SOURCE(S): MARPAT 133:329627
GI




I

AB A compd. of formula I (R0 = H, halogen, C1-6 alkyl; R1 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, halo-C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-3 alkyl, aryl-C1-3 alkyl, heteroaryl-C1-3 alkyl; R2 = (substituted) monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine, or (substituted) bicyclic ring (a) attached to the rest of the mol. via one of the benzene ring carbon atoms, and wherein the fused ring is a 5- or 6-membered ring which may be satd. or partially or fully unsatd., and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur, and nitrogen; R3 = H, C1-3 alkyl, or R1 and R3 together = 3- or 4-membered alkyl or alkenyl chain) and salts and solvates thereof is disclosed. Compd. I is a potent and selective inhibitor of cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase, having a utility in a variety of therapeutic areas where such inhibition is beneficial, including the treatment of

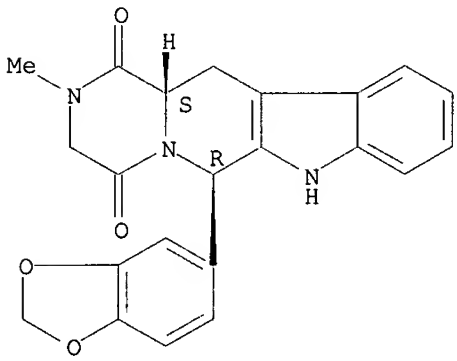
cardiovascular disorders and erectile dysfunction. Thus, many I compds. were synthesized and tested in vitro as inhibitors of cGMP phosphodiesterase. Cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione showed IC50 of 10 nM.

IT **171488-01-0P 171488-03-2P 171488-04-3P**
**171488-06-5P 171488-07-6P 171488-08-7P**
**171488-09-8P 171488-10-1P 171488-11-2P**
**171488-12-3P 171488-13-4P 171488-14-5P**
**171488-15-6P 171488-16-7P 171488-17-8P**
**171488-18-9P 171488-19-0P 171488-20-3P**
**171488-21-4P 171488-22-5P 171488-76-9P**
**171488-77-0P 171488-86-1P 171488-87-2P**
**171488-91-8P 171488-92-9P 171488-94-1P**
**171488-95-2P 171489-01-3P 171489-02-4P**
**171596-27-3P 171596-28-4P 171596-29-5P**
**171596-30-8P 171596-31-9P 171596-32-0P**
**171596-36-4P 171596-39-7P 171596-40-0P**
**187935-15-5P 303984-32-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tetracyclic cyclic GMP-specific phosphodiesterase inhibitors and their use in disease treatment)

RN 171488-01-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

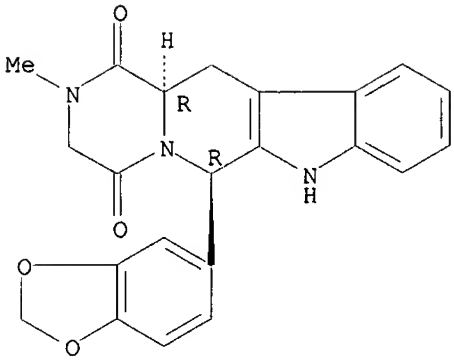
Relative stereochemistry.




RN 171488-03-2 CAPLUS

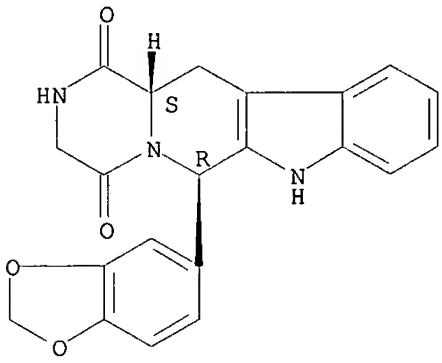
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



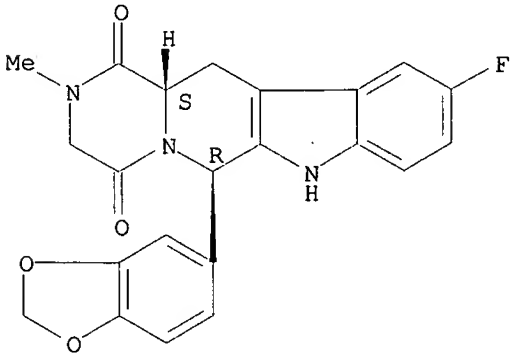
RN 171488-04-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-06-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-10-fluoro-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

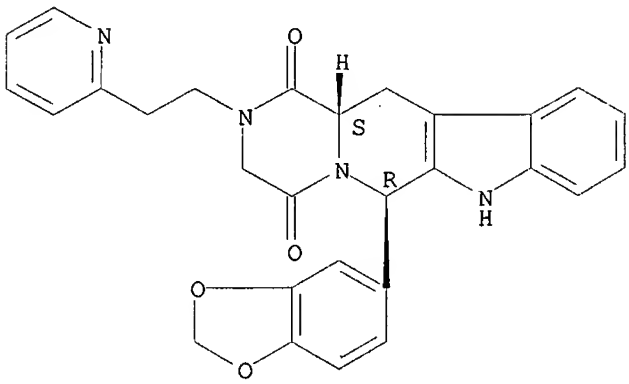
Relative stereochemistry.



RN 171488-07-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-

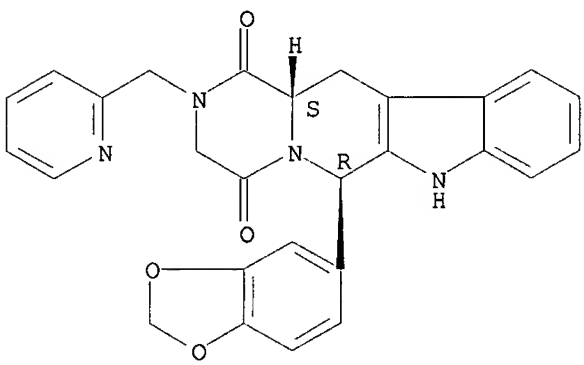
2,3,6,7,12,12a-hexahydro-2-[2-(2-pyridinyl)ethyl]-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



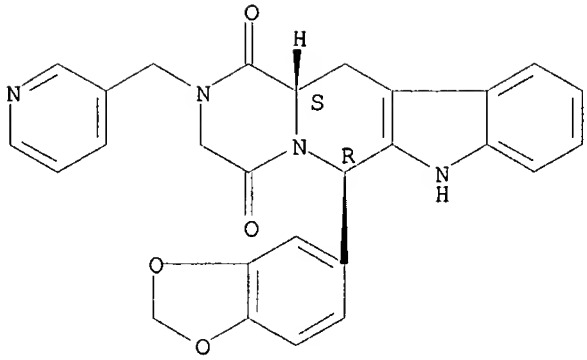
RN 171488-08-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



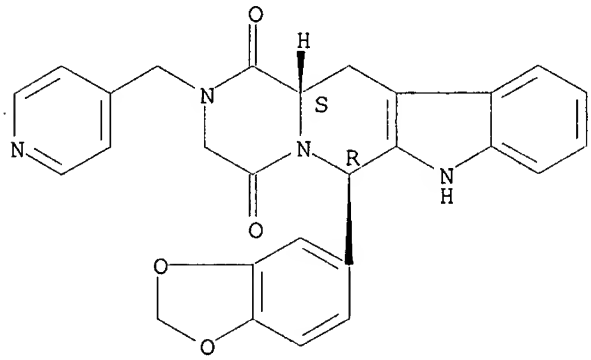
RN 171488-09-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



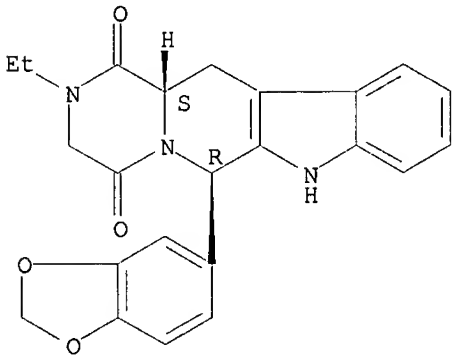
RN 171488-10-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(4-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-11-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-ethyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

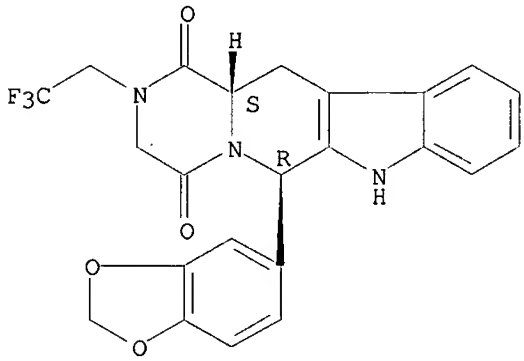
Relative stereochemistry.



RN 171488-12-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-

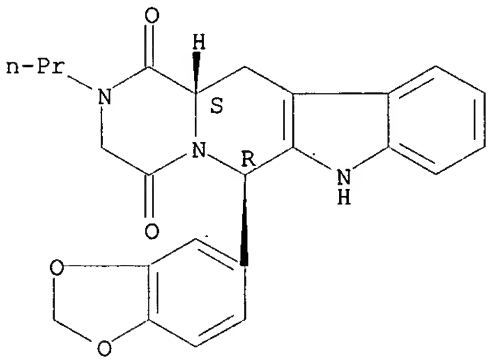
2,3,6,7,12,12a-hexahydro-2-(2,2,2-trifluoroethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



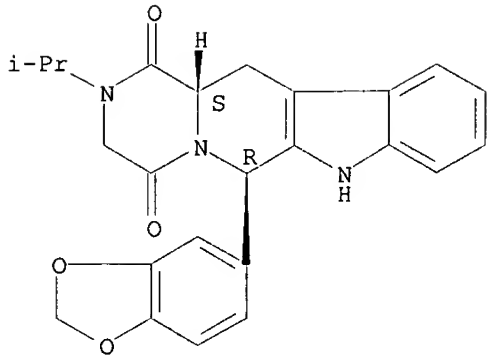
RN 171488-13-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-propyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



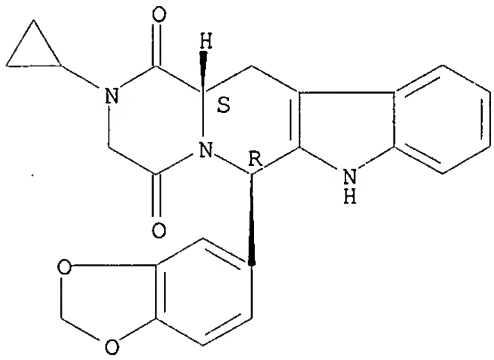
RN 171488-14-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



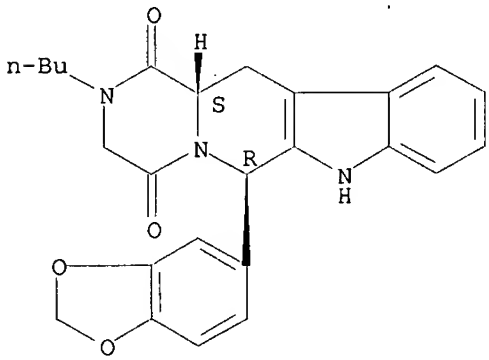
RN 171488-15-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopropyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-16-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

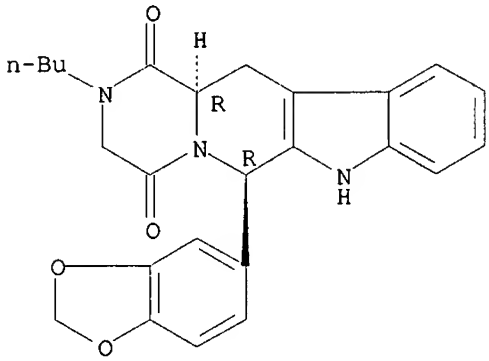
Relative stereochemistry.



RN 171488-17-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-

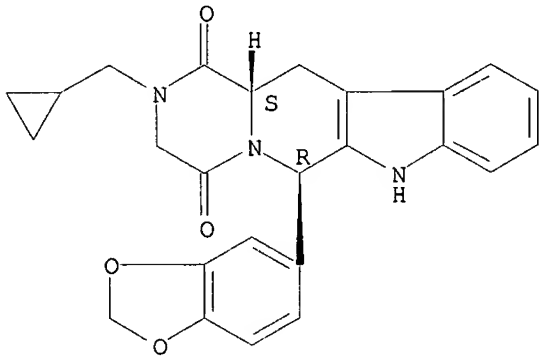
2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



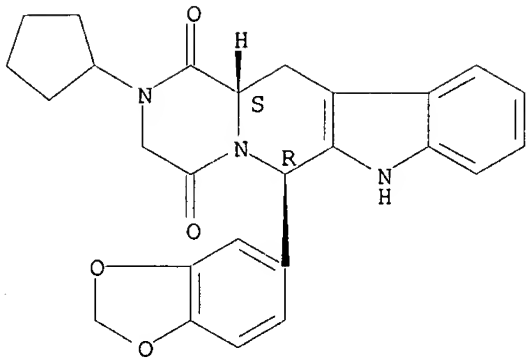
RN 171488-18-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclopropylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



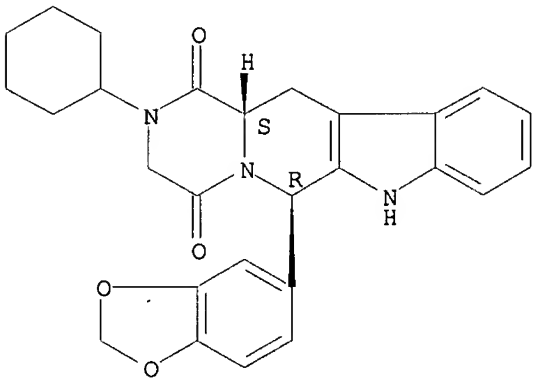
RN 171488-19-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



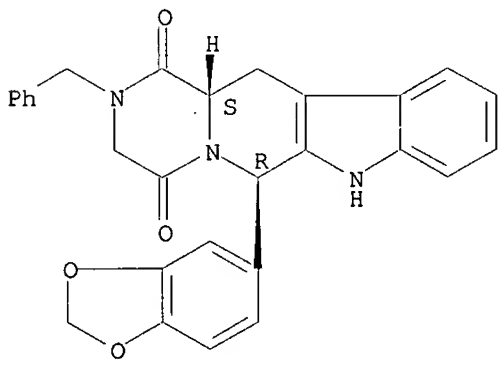
RN 171488-20-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclohexyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



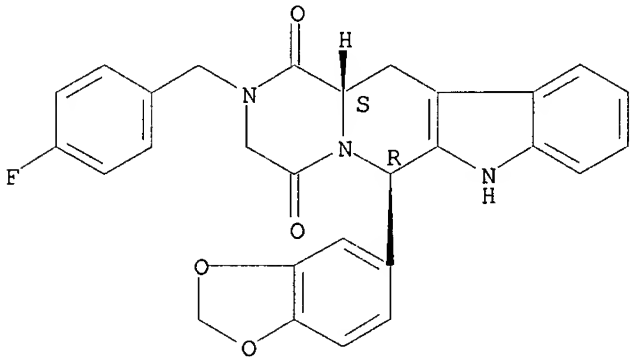
RN 171488-21-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(phenylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



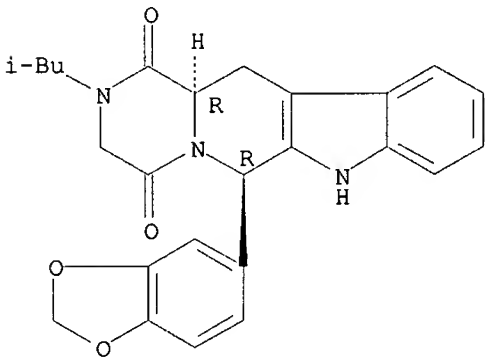
RN 171488-22-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(4-fluorophenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



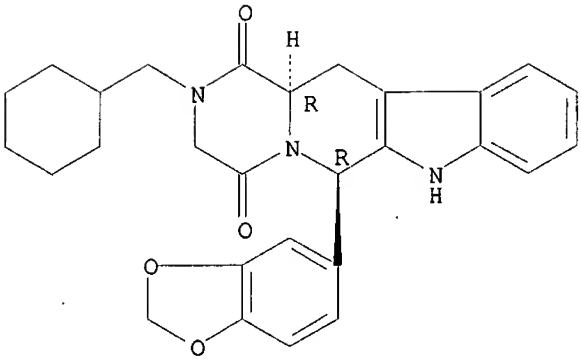
RN 171488-76-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-methylpropyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



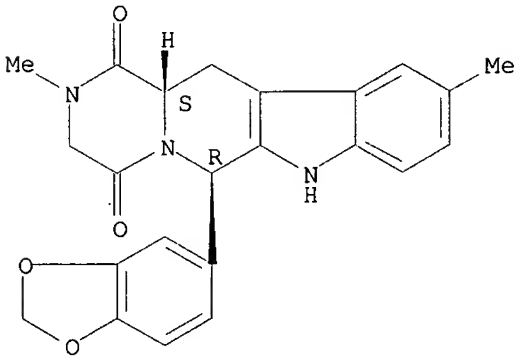
RN 171488-77-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclohexylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



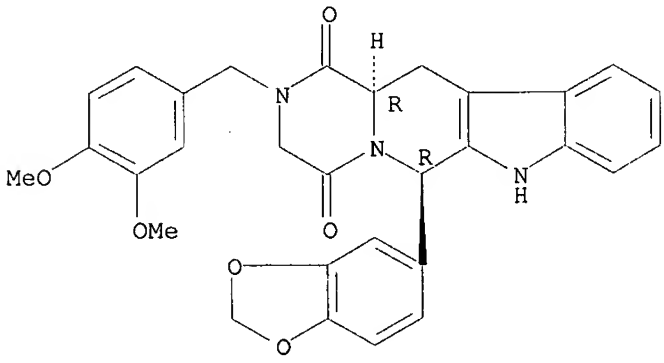
RN 171488-86-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,10-dimethyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-87-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(3,4-dimethoxyphenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

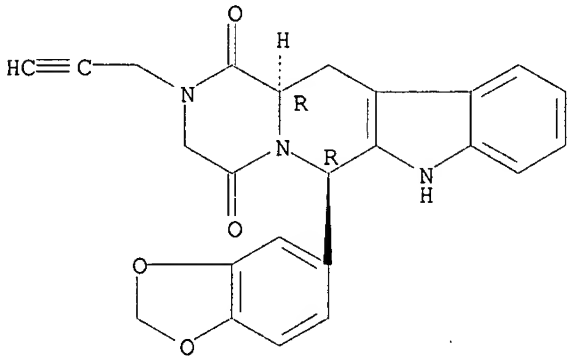
Absolute stereochemistry. Rotation (+).



RN 171488-91-8 CAPLUS

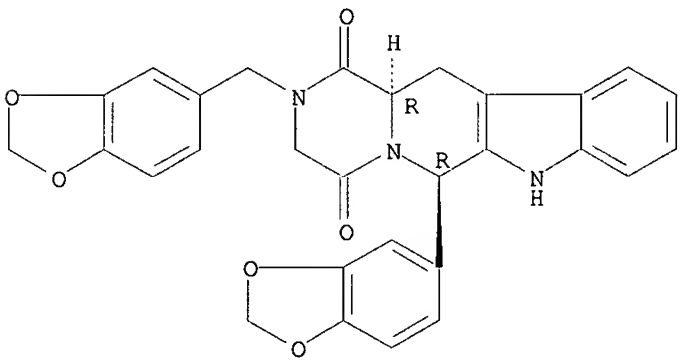
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-propynyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



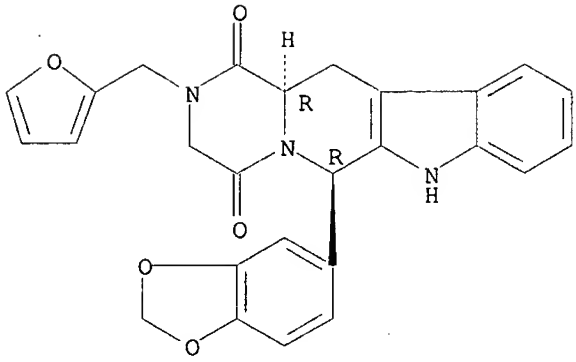
RN 171488-92-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(1,3-benzodioxol-5-ylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



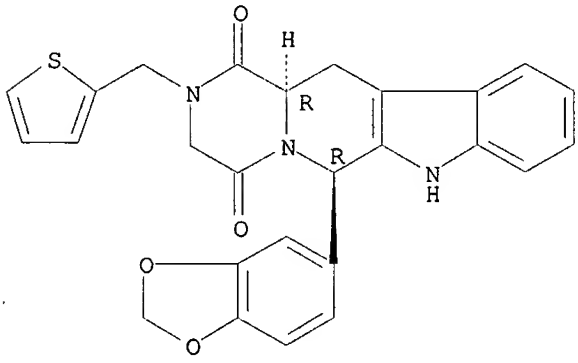
RN 171488-94-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(2-furanylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



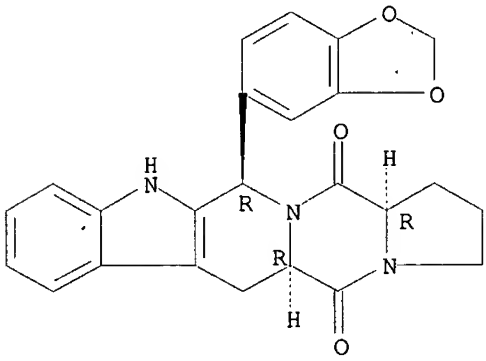
RN 171488-95-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-thienylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171489-01-3 CAPLUS
CN 5H,14H-Pyrrolo[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-5,14-dione, 12-(1,3-benzodioxol-5-yl)-1,2,3,5a,6,11,12,14a-octahydro-, (5aR,12R,14aR)- (9CI) (CA INDEX NAME)

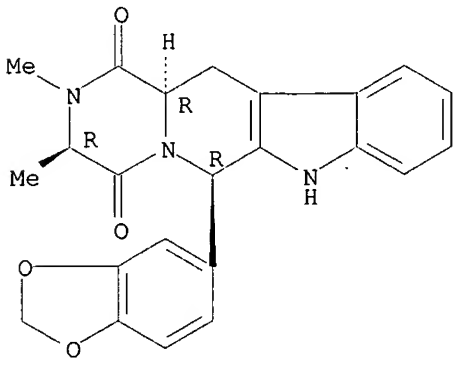
Absolute stereochemistry. Rotation (+).



RN 171489-02-4 CAPLUS

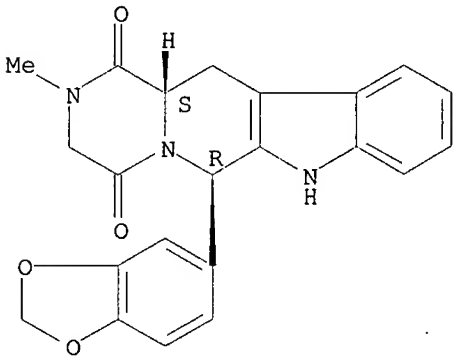
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



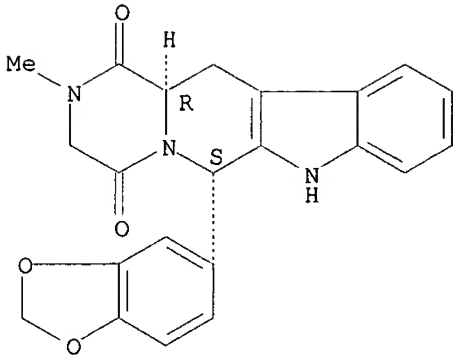
RN 171596-27-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



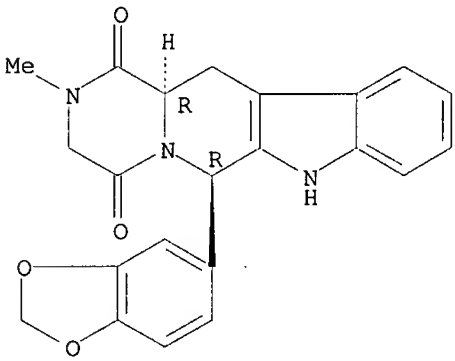
RN 171596-28-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6S,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



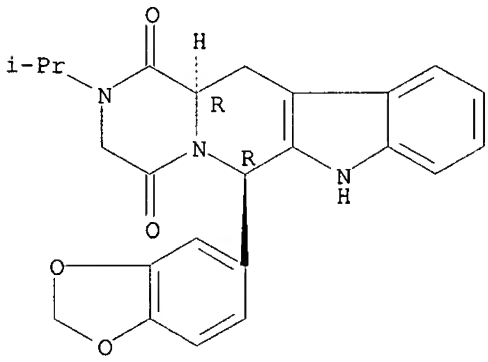
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-30-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

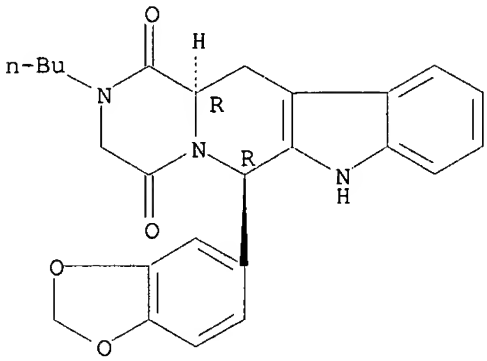
Absolute stereochemistry. Rotation (+).



RN 171596-31-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-

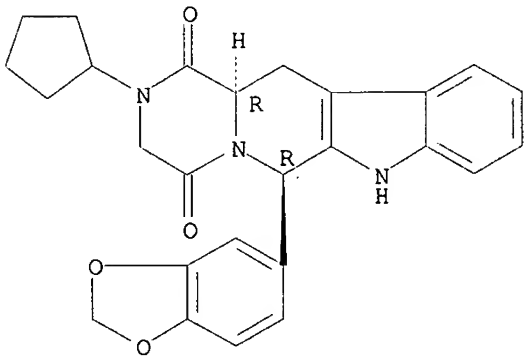
2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



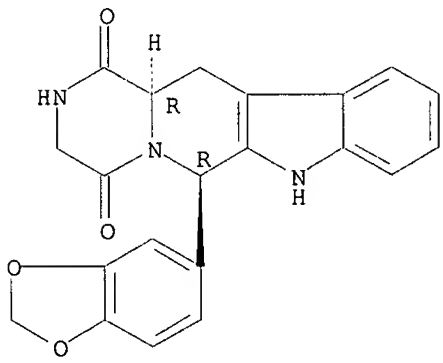
RN 171596-32-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



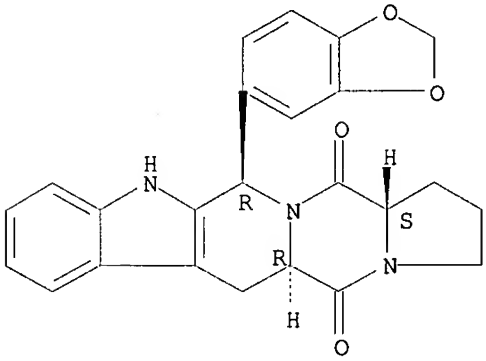
RN 171596-36-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



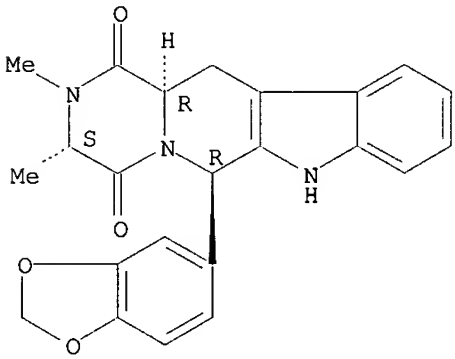
RN 171596-39-7 CAPLUS
CN 5H,14H-Pyrrolo[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-5,14-dione, 12-(1,3-benzodioxol-5-yl)-1,2,3,5a,6,11,12,14a-octahydro-, (5aR,12R,14aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



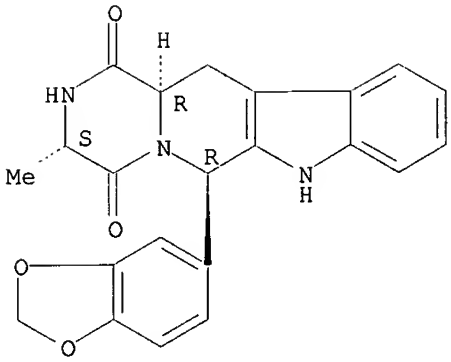
RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



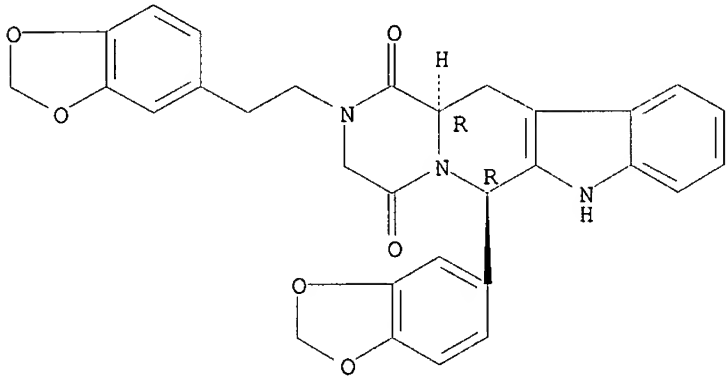
RN 187935-15-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-methyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 303984-32-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(1,3-benzodioxol-5-yl)ethyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:686171 CAPLUS
DOCUMENT NUMBER: 133:271672
TITLE: Phosphodiesterase inhibitor preparation for treatment of sexual functional disorders
PATENT ASSIGNEE(S): Lilly Icos Llc, USA
SOURCE: Ger. Gebrauchsmusterschrift, 47 pp.
CODEN: GGXXFR
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 20007861 | U1 | 20000928 | DE 2000-20007861 | 20000426 |
| NO 2000002097 | A | 20011026 | NO 2000-2097 | 20000425 |
| CA 2307101 | AA | 20001030 | CA 2000-2307101 | 20000426 |
| FI 2000000976 | A | 20001030 | FI 2000-976 | 20000426 |

| | | | | | |
|---|---|---|---|---|---|
| NL 1015027 | A1 | 20001031 | NL 2000-1015027 | 20000426 | |
| NL 1015027 | C2 | 20010214 | | | |
| SE 2000001518 | A | 20001031 | SE 2000-1518 | 20000426 | |
| ZA 2000002058 | A | 20001102 | ZA 2000-2058 | 20000426 | |
| WO 2000066099 | A2 | 20001109 | WO 2000-US11129 | 20000426 | |
| WO 2000066099 | A3 | 20010118 | | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| DE 10021266 | A1 | 20001116 | DE 2000-10021266 | 20000426 |
| JP 2000336043 | A2 | 20001205 | JP 2000-126472 | 20000426 |
| FR 2795646 | A1 | 20010105 | FR 2000-5296 | 20000426 |
| GB 2351663 | A1 | 20010110 | GB 2000-10199 | 20000426 |
| LT 4758 | B | 20010226 | LT 2000-35 | 20000426 |
| LV 12560 | B | 20010420 | LV 2000-56 | 20000426 |
| CN 1292264 | A | 20010425 | CN 2000-106987 | 20000426 |
| BE 1012957 | A5 | 20010605 | BE 2000-295 | 20000426 |
| EP 1173181 | A2 | 20020123 | EP 2000-926367 | 20000426 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

| | | | | |
|---|---|---|---|---|
| LU 90569 | A2 | 20020227 | LU 2000-90569 | 20000426 |
| NO 2001005275 | A | 20011206 | NO 2001-5275 | 20011029 |

PRIORITY APPLN. INFO.: US 1999-132036P P 19990430
WO 2000-US11129 W 20000426

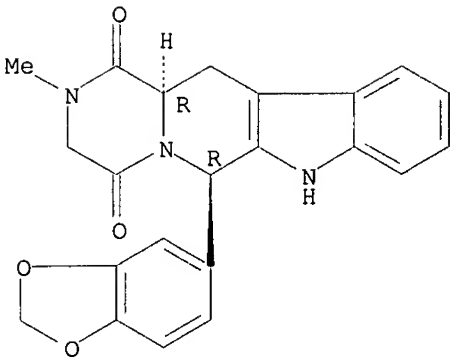
AB A formulation for the treatment of sexual malfunctions (e.g., erectile dysfunction in men and decreased libido in women) which contains a phosphodiesterase 5 inhibitor with a IC50 of at least 100-fold lower than that with phosphodiesterase 6 as active ingredient, and which inhibits phosphodiesterase 5 with an IC50 of at least 1000-fold lower than for phosphodiesterase 1c and a IC50 for PDE5 of below 10 nM.

IT **171596-29-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(phosphodiesterase inhibitor prepn. for treatment of sexual functional disorders)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L12 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:666601 CAPLUS
DOCUMENT NUMBER: 133:256811
TITLE: Pharmaceutical compositions containing dopamine agonists in combination with nitric oxide donors for treating and/or preventing sexual dysfunctions
INVENTOR(S): Garvey, David S.
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000054773 | A1 | 20000921 | WO 2000-US3709 | 20000310 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-123920P P 19990312
OTHER SOURCE(S): MARPAT 133:256811

AB The present invention is directed to novel compns. comprising at least one dopamine agonist in combination with at least one nitric oxide donor (i.e. compds. that donate, transfer or release nitric oxide, elevate endogenous levels of endothelium-derived relaxing factor, stimulate endogenous synthesis of nitric oxide or are substrates for nitric oxide synthase). The novel compns. may optionally comprise at least one therapeutic agent, such as, a vasoactive agent, an antiemetic agent, and mixts. thereof. The dopamine agonist is preferably apomorphine. The present invention is also directed to methods for treating and/or preventing sexual dysfunctions and/or enhancing sexual responses in patients. In other embodiments, the present invention is directed to methods treating or preventing neurodegenerative diseases, mitochondrial diseases, spinal cord injury, central or psychostimulant addiction, senile dementia, circulatory disorders, cardiovascular disorders, hyperprolactinemia or myopia. The compds. and/or compns. of the present invention can also be provided in

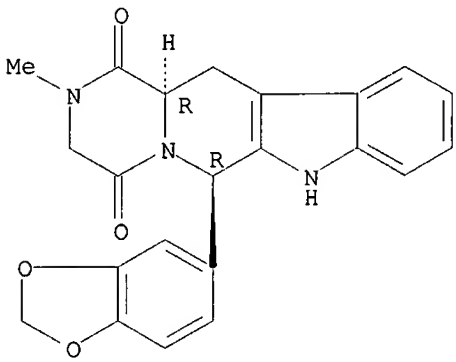
the form of a pharmaceutical kit (no data).

IT **171596-29-5**, Ic 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. dopamine agonists in combination with nitric oxide donors for treating and/or preventing sexual dysfunctions)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:645819 CAPLUS
DOCUMENT NUMBER: 133:227820
TITLE: Pharmaceutical compositions for treating erectile dysfunction containing a melanocortin receptor agonist and a cyclic-GMP-specific phosphodiesterase inhibitor or an .alpha.-adrenergic receptor antagonist
INVENTOR(S): Stoner, Elizabeth
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Waldstreicher, Joanne
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000053148 | A2 | 20000914 | WO 2000-US5711 | 20000303 |
| WO 2000053148 | A3 | 20001214 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1161255 | A2 | 20011212 | EP 2000-916081 | 20000303 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-123244P P 19990308
WO 2000-US5711 W 20000303

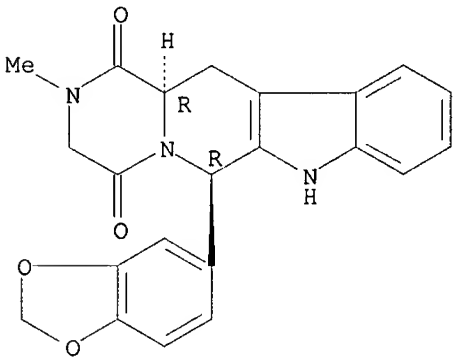
AB The present invention provides for a method for the treatment of erectile dysfunction in a male or female human subject in need of such treatment comprising administration of a therapeutically effective amt. of an agonist of the melanocortin receptor in combination with a therapeutically effective amt. of a cyclic-GMP-specific phosphodiesterase inhibitor or an alpha-adrenergic receptor antagonist. Further, the present invention provides for pharmaceutical compns. useful in the methods of the present invention, as well as a method of manuf. of a medicament useful for treating erectile dysfunction. Effect of the combination of 20 mg/kg of the invention compds. was tested in rats. A hard gelatin capsule contained a melanocortin receptor agonist 5, and a type V phosphodiesterase inhibitor 10 mg.

IT **171596-29-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for treating erectile dysfunction contg. melanocortin receptor agonist and cyclic-GMP-specific phosphodiesterase inhibitor or .alpha.-adrenergic receptor antagonist)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

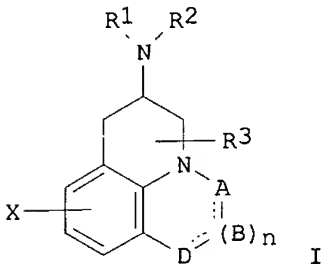
Absolute stereochemistry. Rotation (+).




L12 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:475525 CAPLUS
DOCUMENT NUMBER: 133:109946
TITLE: Methylaminodihydroimidazoquinolinones for treating sexual disturbances and inducing mating in animals
INVENTOR(S): Meglasson, Martin Durham; McCall, Robert B.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

WO 2000040226 A2 20000713 WO 1999-US27951 19991220
WO 2000040226 A3 20010201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
BR 9916759 A 20010925 BR 1999-16759 19991220
EP 1140092 A2 20011010 EP 1999-967142 19991220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-114840P P 19990106
US 1999-115051P P 19990108
US 1999-115922P P 19990114
US 1999-120543P P 19990217
WO 1999-US27951 W 19991220
OTHER SOURCE(S): MARPAT 133:109946
GI



I

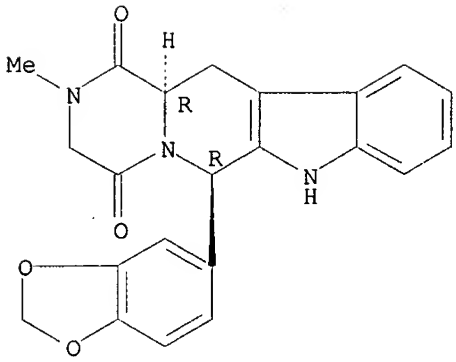
AB The present invention is a method of treating sexual disturbances in humans and inducing mating in non-human mammals using the compds. of formula (I: R1,R2,R3 = H, alkyl, alkenyl, cycloalkyl, etc.; X = H, alkyl, halogen, OH, etc.; A,B,D = CH, CH2, CO, N, etc.; n = 0 or 1) in a dosage range where the sexually therapeutic amt. is from about 0.2 through 8 mg/person/dose and where the sexually mating amt. is from about 0.003 through 0.2 mg/kg/dose.

IT **171596-29-5**, ICOS 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(treating sexual disturbances and inducing mating in animals)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

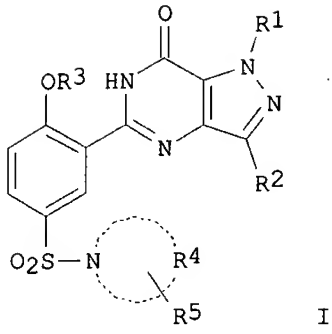
Absolute stereochemistry. Rotation (+).



L12 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:392967 CAPLUS
DOCUMENT NUMBER: 133:22405
TITLE: Preventives containing 1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one derivatives and related compounds for nitric acid-induced tolerance
INVENTOR(S): Ellis, Peter
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2000159672 | A2 | 20000613 | JP 1999-337606 | 19991129 |
| US 6225315 | B1 | 20010501 | US 1999-442821 | 19991118 |
| EP 1022026 | A2 | 20000726 | EP 1999-309406 | 19991125 |
| EP 1022026 | A3 | 20020410 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| AU 9961788 | A1 | 20000601 | AU 1999-61788 | 19991130 |
| KR 2000035774 | A | 20000626 | KR 1999-53785 | 19991130 |

PRIORITY APPLN. INFO.: US 1998-110335P P 19981130
OTHER SOURCE(S): MARPAT 133:22405
GI



I

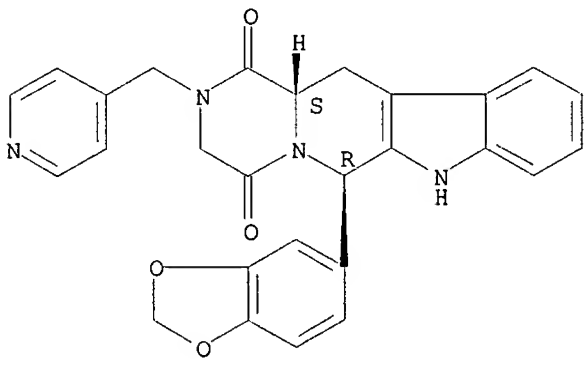
AB The title compds. [I; R1 = H, C1-3 alkyl, C3-5 cycloalkyl, C1-3 perfluoroalkyl; R2 = H, C1-3 perfluoroalkyl, C1-6 alkyl substituted by OH, C1-3 alkoxy, or C3-6 cycloalkyl; R3 = C1-6 alkyl, C3-6 alkenyl, C3-6 alkynyl, C3-7 cycloalkyl, C1-6 perfluoroalkyl, C3-6 cycloalkyl-C1-6 alkyl; R4 together with the R4-bonded N completes 4-N-R6-piperazinyl; R5 = H, C1-4 alkyl, C1-3 alkoxy, NR7R8, CONR7R8; wherein R6 = H, C1-6 alkyl, hydroxy-C2-6 alkyl, R7R8N-C2-6 alkyl, R7R8NCO-C1-6 alkyl, CONR7R8, CSNR7R8, C(:NH)NR7R8; wherein R7, R8 = H, C1-4 alkyl, C1-3 alkoxy-C2-4 alkyl, hydroxy-C2-4 alkyl], pharmacol. acceptable salts, prodrugs, polymorphs, hydrates, solvates, active metabolites, or stereoisomers thereof , which are cGMP phosphodiesterase inhibitors and useful for the prevention of nitrate tolerance (no data), are prepd. The title compds. also include pyrazolo[3,4-d]pyrimidin-4-one, quinazolin-4-one, purin-6-one, pyrido[3,2-d]pyrimidin-4-one, and pyrazino[1',2':1,6]pyrido[3,4-b]indole derivs.

IT **171488-10-1P 171488-15-6P 171596-29-5P 171596-30-8P 171596-32-0P 171596-36-4P 171596-40-0P 187935-15-5P 273207-76-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preventives contg. 1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one derivs. and related compds. as cGMP phosphodiesterase inhibitors for nitric acid-induced tolerance)

RN 171488-10-1 CAPLUS

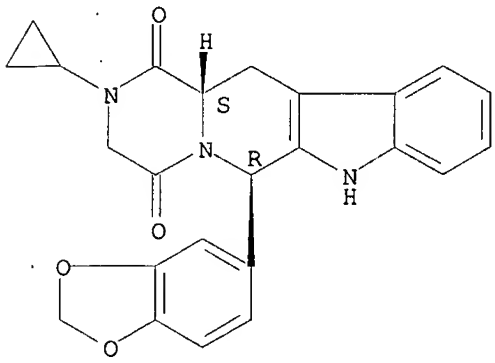
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(4-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



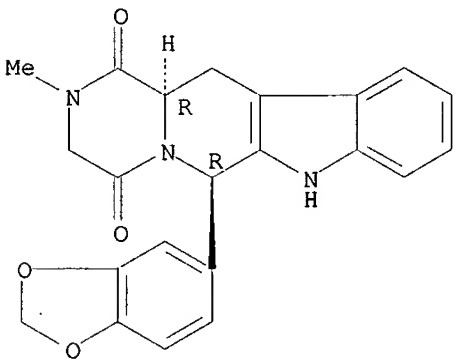
RN 171488-15-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopropyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



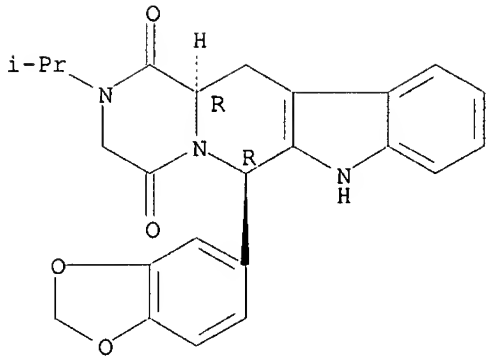
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



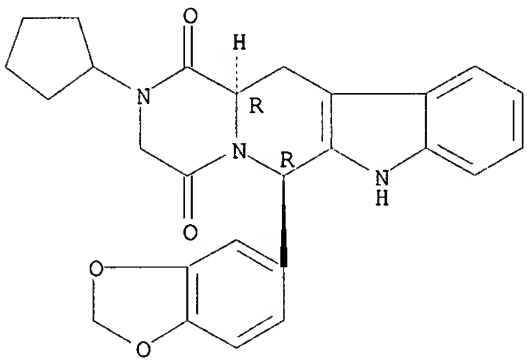
RN 171596-30-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



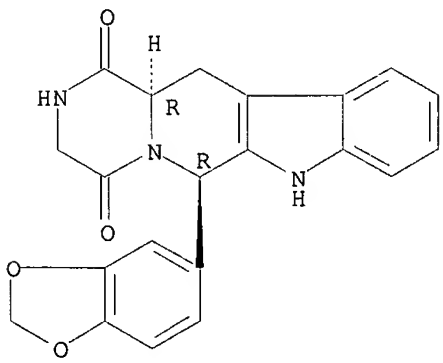
RN 171596-32-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-36-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

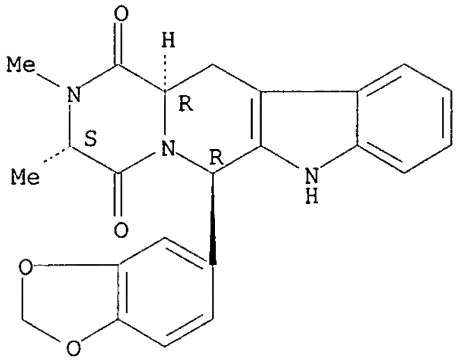
Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX

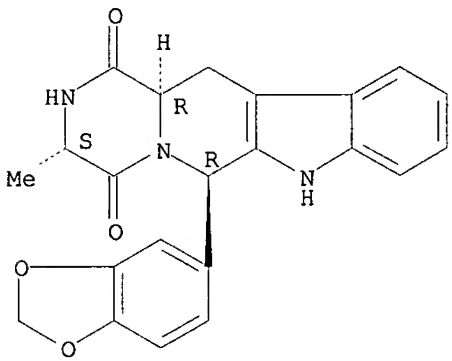
NAME)

Absolute stereochemistry. Rotation (+).



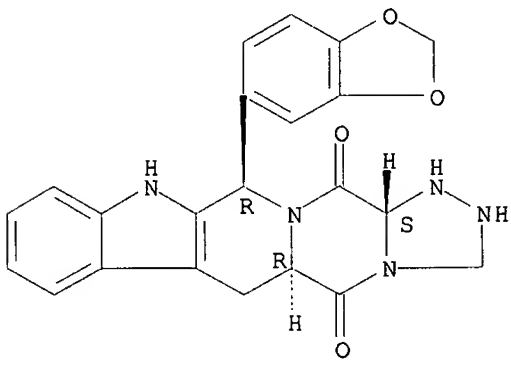
RN 187935-15-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-methyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 273207-76-4 CAPLUS
CN 5H,14H-1,2,4-Triazolo[4'',3'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-5,14-dione, 12-(1,3-benzodioxol-5-yl)-1,2,3,5a,6,11,12,14a-octahydro-, (5aR,12R,14aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:240994 CAPLUS
DOCUMENT NUMBER: 132:270098
TITLE: Tablets immediately disintegrating in the oral cavity
INVENTOR(S): Furitsu, Hisao; Kato, Akira; Ohwaki, Takayuki; Yasui, Masanori
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

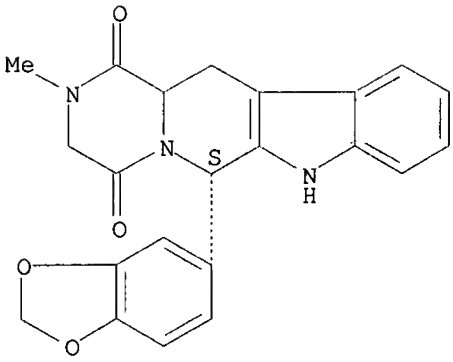
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000020033 | A1 | 20000413 | WO 1999-JP5298 | 19990928 |
| W: CA, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 1120120 | A1 | 20010801 | EP 1999-944874 | 19990928 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2000178204 | A2 | 20000627 | JP 1999-276133 | 19990929 |
| JP 2000191518 | A2 | 20000711 | JP 1999-276134 | 19990929 |

PRIORITY APPLN. INFO.: JP 1998-282378 A 19981005
JP 1998-295947 A 19981019
WO 1999-JP5298 W 19990928
OTHER SOURCE(S): MARPAT 132:270098

AB The invention relates to tablets immediately disintegrating in the oral cavity which contain a phosphodiesterase inhibitor having an effect of ameliorating erectile dysfunction and a process for producing the same; and tablets immediately disintegrating in the oral cavity which contain a hardly sol. drug and show an improved soly.; and a process for producing the same. Namely, tablets immediately disintegrating in the oral cavity which contain a cyclic GMP phosphodiesterase inhibitor [e.g. sildenafil] and saccharides and process for producing the same; and a process for producing tablets immediately disintegrating in the oral cavity which comprises dissolving the hardly sol. drug together with a surfactant and/or a water-sol. polymer in an org. solvent or an aq. org. solvent, mixing saccharides with a molded matter obtained by coating a filler or granulating together with a filler, adding an org. solvent, water or an aq. org. solvent thereto, kneading the resultant mixt. and then compression molding the same.

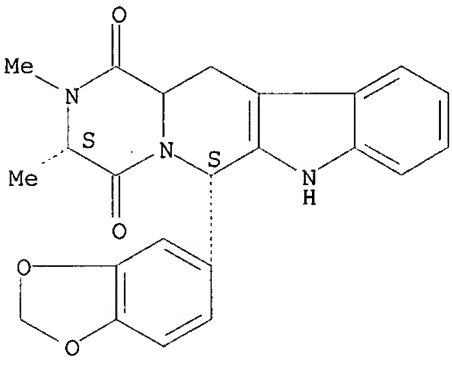
IT **263392-02-5 263392-03-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tablets immediately disintegrating in the oral cavity)
RN 263392-02-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 263392-03-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:753072 CAPLUS
DOCUMENT NUMBER: 131:346565
TITLE: Combination of phentolamine and cyclic GMP phosphodiesterase inhibitors for the treatment of sexual dysfunction
INVENTOR(S): Estok, Thomas Mark
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9959584 | A1 | 19991125 | WO 1999-US7046 | 19990517 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT,

RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

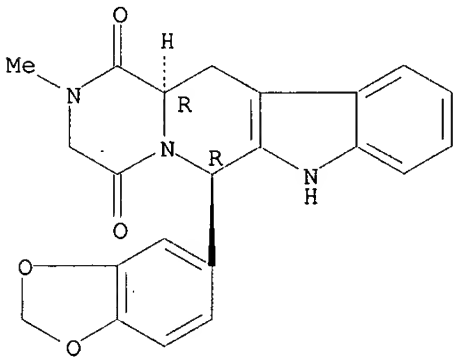
AU 9940685 A1 19991206 AU 1999-40685 19990517
PRIORITY APPLN. INFO.: US 1998-81640 A 19980520
US 1998-82977 A2 19980521
US 1998-106517 A 19980629
WO 1999-US7046 W 19990517

AB A method of treating sexual dysfunction comprising administering a therapeutically effective amt. of a combination of phentolamine and cGMP PDE inhibitor (e.g. sildenafil), as well as pharmaceutical compns. and kits useful in those methods, are disclosed.

IT **171596-29-5 171596-40-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phentolamine and cyclic GMP phosphodiesterase inhibitors for the treatment of sexual dysfunction)

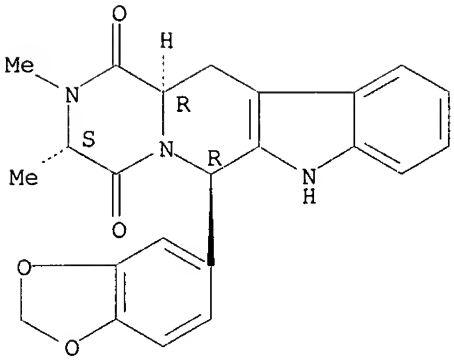
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

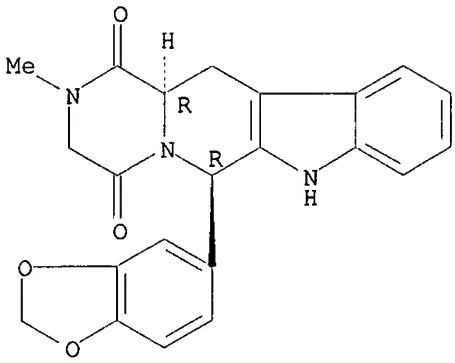
L12 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:393867 CAPLUS
DOCUMENT NUMBER: 131:193591
TITLE: IC-351 ICOS Corp
AUTHOR(S): Norman, Peter
CORPORATE SOURCE: Norman Consulting, Bucks, SL1 8JW, UK
SOURCE: Current Opinion in Central & Peripheral Nervous System Investigational Drugs (1999), 1(2), 268-271
CODEN: COCDFA; ISSN: 1464-844X
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 35 refs. IC-351 (GF-196960), an inhibitor of phosphodiesterase 5 (PDE5) from ICOS Corp, is in phase II trials for the treatment of mild to moderate erectile dysfunction (ED) [274568], [296831]. A randomized, placebo-controlled, crossover study assessed the safety and physiol. effects of IC-351 in patients with ED [274568]. Enrollment was completed in Apr. 1998 [284935]. Results from the trial showed that IC-351 demonstrated significant benefit over placebo [311566]. In Oct. 1998, ICOS entered into a joint venture agreement with Eli Lilly for the development and commercialization of IC-351 for the treatment of sexual dysfunction [300118], [310951]. IC-351 is also in development for the treatment of female sexual dysfunction [321995]. In Mar. 1998, the company announced that the compd. was in preclin. evaluation for the treatment of hypertension [284638]. A collaboration with Glaxo Wellcome (GW) was terminated in Mar. 1997 [240438] and intellectual property rights were assigned to ICOS. This left ICOS to develop the compds. with royalties payable to GW. Although GW reserved the right to pursue its own program, it does not appear to be doing so. In Feb. 1999 Deutsche Bank predicted sales of $200 million in 2002 rising to $400 million in 2003 for IC-351 [316821].

IT **171596-29-5**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(effect of IC-351 for treatment of mild to moderate erectile dysfunction)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:215760 CAPLUS
DOCUMENT NUMBER: 126:203727
TITLE: Use of cGMP-phosphodiesterase inhibitors to treat impotence
INVENTOR(S): Daugan, Alain Claude-Marie
PATENT ASSIGNEE(S): Laboratoire Glaxo Wellcome S.A., Fr.; Daugan, Alain Claude-Marie
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9703675 | A1 | 19970206 | WO 1996-EP3024 | 19960711 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA | | | | |
| CA 2226784 | AA | 19970206 | CA 1996-2226784 | 19960711 |
| AU 9664191 | A1 | 19970218 | AU 1996-64191 | 19960711 |
| AU 704955 | B2 | 19990513 | | |
| EP 839040 | A1 | 19980506 | EP 1996-923985 | 19960711 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI | | | | |
| CN 1195290 | A | 19981007 | CN 1996-196723 | 19960711 |
| BR 9609758 | A | 19990126 | BR 1996-9758 | 19960711 |
| JP 11509221 | T2 | 19990817 | JP 1996-506248 | 19960711 |
| CZ 289686 | B6 | 20020313 | CZ 1998-33 | 19960711 |
| NO 9800153 | A | 19980310 | NO 1998-153 | 19980113 |
| US 6140329 | A | 20001031 | US 1998-981989 | 19980310 |
| US 6143746 | A | 20001107 | US 1998-154051 | 19980916 |

PRIORITY APPLN. INFO.:
GB 1995-14464 A 19950714
GB 1994-1090 A 19940121
WO 1995-EP183 A2 19950119
GB 1995-14465 A 19950714

WO 1996-EP3024 W 19960711
WO 1996-EP3025 A2 19960711

OTHER SOURCE(S): MARPAT 126:203727

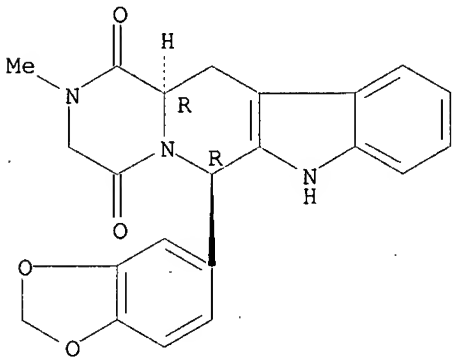
AB Compds. such as (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione, (3S,6R,12aR)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione, and physiol. acceptable salts and solvates thereof, can be used as cGMP-phosphodiesterase inhibitors in the treatment of impotence.

IT **171596-29-5P 171596-40-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cGMP-phosphodiesterase inhibitor formulations to treat impotence)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

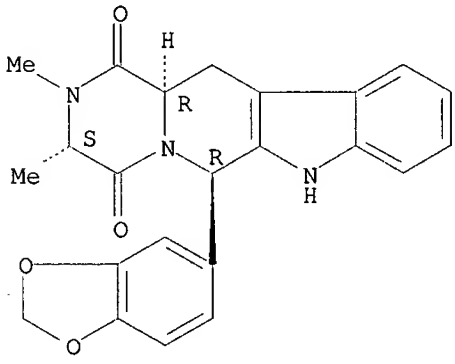
Absolute stereochemistry. Rotation (+).




RN 171596-40-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

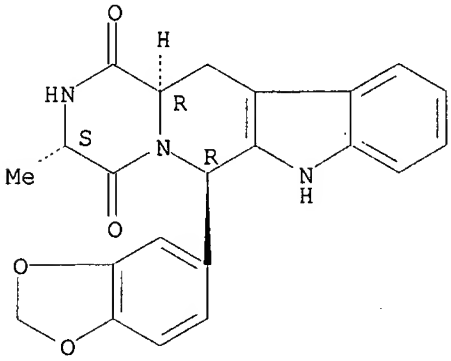
Absolute stereochemistry. Rotation (+).




IT **187935-15-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cGMP-phosphodiesterase inhibitor formulations to treat impotence)

RN 187935-15-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-methyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L12 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:101617 CAPLUS
DOCUMENT NUMBER: 126:108935
TITLE: Method of producing a solid dispersion of a poorly water-soluble drug
INVENTOR(S): Butler, James Matthew
PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Butler, James Matthew
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9638131 | A1 | 19961205 | WO 1996-EP2299 | 19960530 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| AU 9660026 | A1 | 19961218 | AU 1996-60026 | 19960530 |
| EP 828479 | A1 | 19980318 | EP 1996-917457 | 19960530 |
| EP 828479 | B1 | 20011024 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AT 207344 | E | 20011115 | AT 1996-917457 | 19960530 |
| US 5985326 | A | 19991116 | US 1998-952938 | 19980206 |

PRIORITY APPLN. INFO.: GB 1995-11220 A 19950602
WO 1996-EP2299 W 19960530

AB A process for prepg. solid dispersions of poorly sol. drugs comprises (1) providing an intimate mixt. contg. the carrier or excipient and a nonaq. water-miscible solvent, and optionally, water, (2) mixing the intimate mixt. with the poorly water-sol. drug, and (3) pptg. the drug and the carrier or excipient. Specifically, solid dispersions of (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione (I)

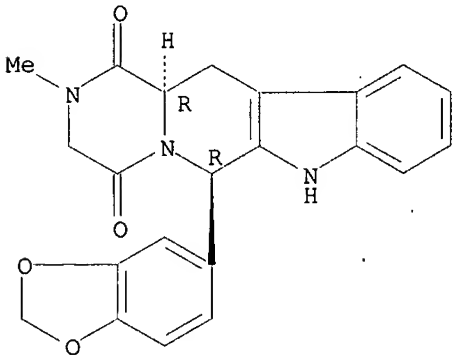
and (+)-N-[1-(adamantanmethyl)-2,4-dioxo-5-phenyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin-3-yl]-N'-phenylurea are described. I 1 g and hydroxypropyl Me cellulose phthalate 1 g were dissolved in a 9:1 mixt. of acetone/water (27 mL) and 0.25 M HCl 83 mL was added to obtain a ppt. The ppt. was filtered, washed with water, dried, and milled. A tablet contg. 100 mg ppt. was formulated.

IT **171596-29-5P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindole deriv. in manuf. of solid dispersion of poorly water-sol. drugs)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




L12 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:986316 CAPLUS
DOCUMENT NUMBER: 124:55977
TITLE: Preparation of pyrazinopyridoindolediones as inhibitors of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase
INVENTOR(S): Daugan, Alain Claude-Marie
PATENT ASSIGNEE(S): Laboratoires Glaxo S.A., Fr.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9519978 | A1 | 19950727 | WO 1995-EP183 | 19950119 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US | | | | |
| RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| TW 378210 | B | 20000101 | TW 1995-84100415 | 19950118 |
| CA 2181377 | AA | 19950727 | CA 1995-2181377 | 19950119 |
| AU 9515748 | A1 | 19950808 | AU 1995-15748 | 19950119 |

| | | | | | |
|---|---|---|---|---|---|
| AU 689205 | B2 | 19980326 | | | |
| ZA 9500424 | A | 19950927 | ZA 1995-424 | 19950119 | |
| EP 740668 | A1 | 19961106 | EP 1995-907565 | 19950119 | |
| EP 740668 | B1 | 19980729 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | | |
| CN 1143963 | A | 19970226 | CN 1995-192078 | 19950119 | |
| CN 1045777 | B | 19991020 | | | |
| HU 74943 | A2 | 19970328 | HU 1996-1982 | 19950119 | |
| JP 09508113 | T2 | 19970819 | JP 1995-519339 | 19950119 | |
| BR 9506559 | A | 19971028 | BR 1995-6559 | 19950119 | |
| AT 169018 | E | 19980815 | AT 1995-907565 | 19950119 | |
| IL 112384 | A1 | 19980816 | IL 1995-112384 | 19950119 | |
| ES 2122543 | T3 | 19981216 | ES 1995-907565 | 19950119 | |
| RU 2142463 | C1 | 19991210 | RU 1996-117127 | 19950119 | |
| CZ 286566 | B6 | 20000517 | CZ 1996-2116 | 19950119 | |
| SK 280879 | B6 | 20000814 | SK 1996-940 | 19950119 | |
| PL 179744 | B1 | 20001031 | PL 1995-315559 | 19950119 | |
| LV 11690 | B | 19970620 | LV 1996-228 | 19960710 | |
| US 5859006 | A | 19990112 | US 1996-669389 | 19960716 | |
| FI 9602927 | A | 19960719 | FI 1996-2927 | 19960719 | |
| NO 9603015 | A | 19960909 | NO 1996-3015 | 19960719 | |
| AU 9873912 | A1 | 19980820 | AU 1998-73912 | 19980626 | |
| AU 707055 | B2 | 19990701 | | | |
| US 6025494 | A | 20000215 | US 1998-133078 | 19980812 | |
| US 6143746 | A | 20001107 | US 1998-154051 | 19980916 | |
| CN 1224720 | A | 19990804 | CN 1998-122779 | 19981201 | |
| CN 1070492 | B | 20010905 | | | |
| US 6127542 | A | 20001003 | US 1999-399667 | 19990921 | |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | GB 1994-1090 | A | 19940121 |
| | WO 1995-EP183 | W | 19950119 |
| | GB 1995-14464 | A | 19950714 |
| | GB 1995-14465 | A | 19950714 |
| | WO 1996-EP3024 | A2 | 19960711 |
| | WO 1996-EP3025 | A2 | 19960711 |
| | US 1996-669389 | A3 | 19960716 |
| | US 1998-133078 | A1 | 19980812 |

OTHER SOURCE(S): MARPAT 124:55977

GI For diagram(s), see printed CA Issue.

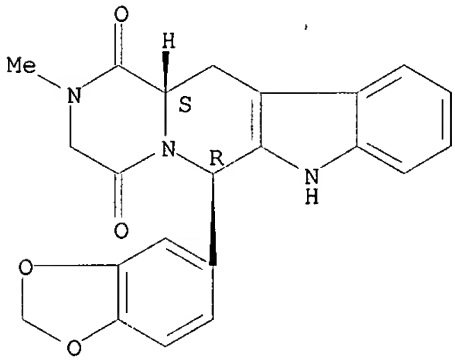
AB The title compds. I [R represents hydrogen, halogen or C1-6 alkyl; R1 represents hydrogen, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, haloC1-6alkyl, C3-8cycloalkyl, etc.; R2 represents an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan and pyridine or an optionally substituted bicyclic ring Q1 attached to the rest of the mol. via one of the benzene ring carbon atoms and wherein the fused ring A is a 5- or 6-membered ring which may be satd. or partially or fully unsatd. and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur and nitrogen; and R3 represents hydrogen or C1-3 alkyl, or R1 and R3 together represent a 3- or 4-membered alkyl or alkenyl chain] are prepd. In an in vitro test for inhibitory effect on cGMP-PDE, cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione (prepn. given) showed IC50 of 10 nM.

IT **171488-01-0P 171488-03-2P 171488-04-3P**
**171488-06-5P 171488-07-6P 171488-08-7P**
**171488-09-8P 171488-10-1P 171488-11-2P**
**171488-12-3P 171488-13-4P 171488-14-5P**
**171488-15-6P 171488-16-7P 171488-17-8P**
**171488-18-9P 171488-19-0P 171488-20-3P**
**171488-21-4P 171488-22-5P 171488-76-9P**
**171488-77-0P 171488-86-1P 171488-87-2P**
**171488-91-8P 171488-92-9P 171488-93-0P**

**171488-94-1P 171488-95-2P 171489-01-3P**
**171489-02-4P 171596-27-3P 171596-28-4P**
**171596-29-5P 171596-30-8P 171596-31-9P**
**171596-32-0P 171596-36-4P 171596-39-7P**
**171596-40-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindolediones as inhibitors of cyclic guanosine monophosphate specific phosphodiesterase)

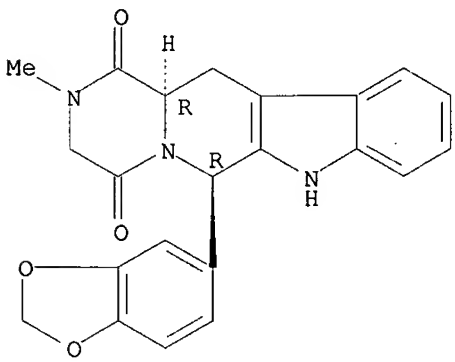
RN 171488-01-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



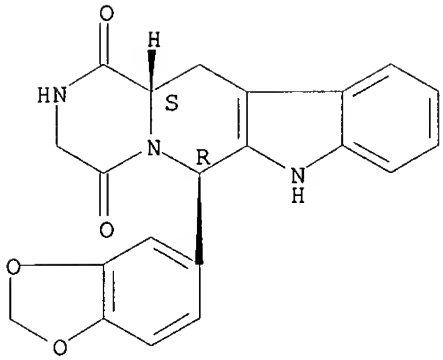
RN 171488-03-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



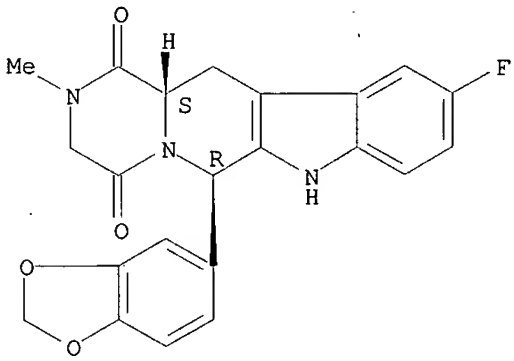
RN 171488-04-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



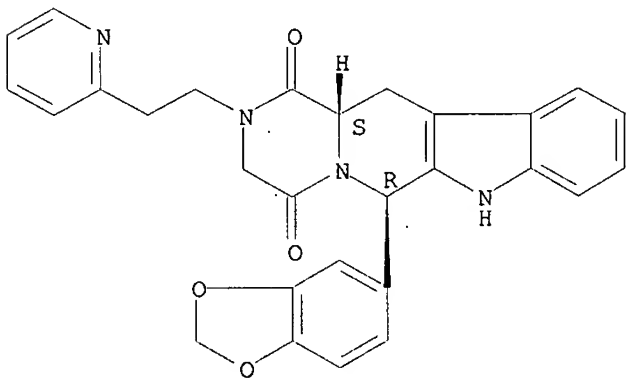
RN 171488-06-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-10-fluoro-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



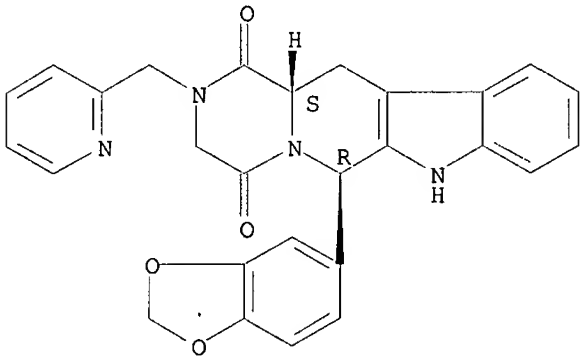
RN 171488-07-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(2-pyridinyl)ethyl]-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



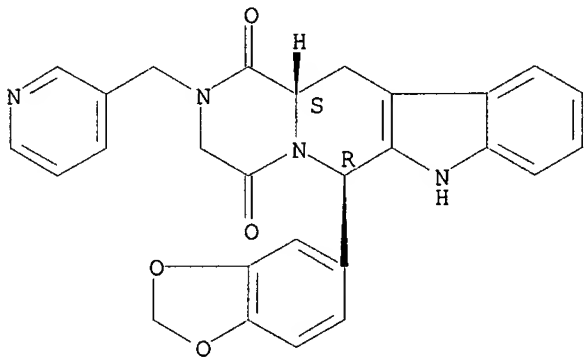
RN 171488-08-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



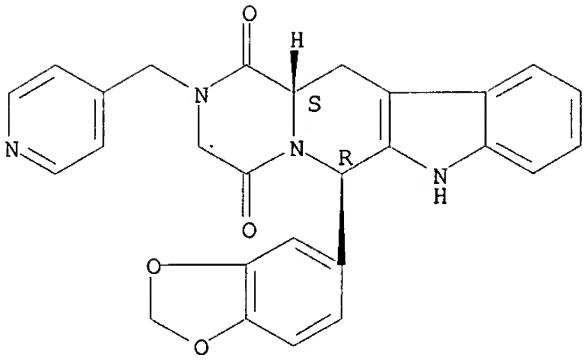
RN 171488-09-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



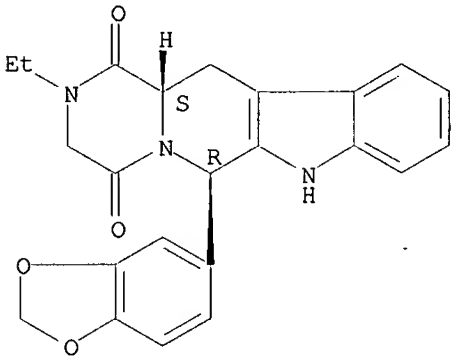
RN 171488-10-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(4-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



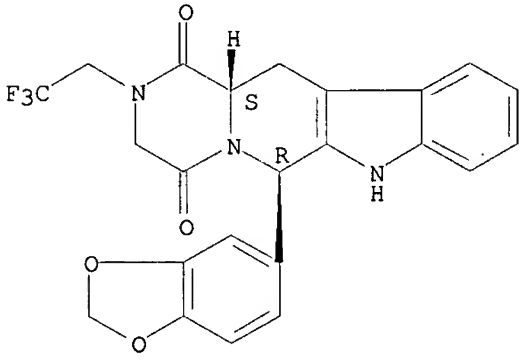
RN 171488-11-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-ethyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-12-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2,2,2-trifluoroethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

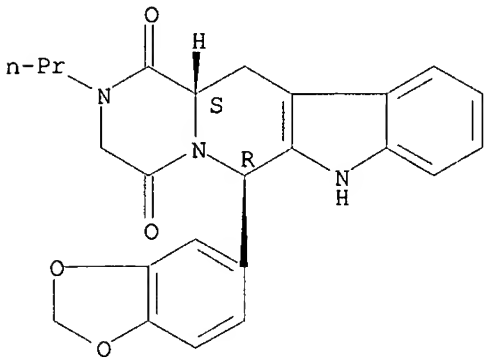
Relative stereochemistry.



RN 171488-13-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-

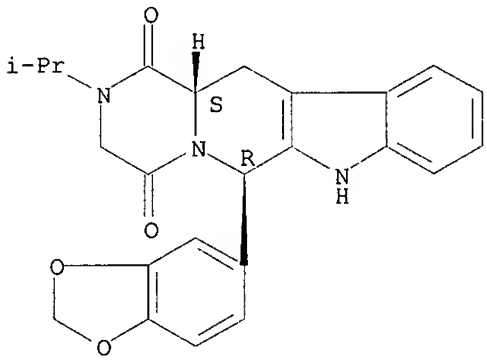
2,3,6,7,12,12a-hexahydro-2-propyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



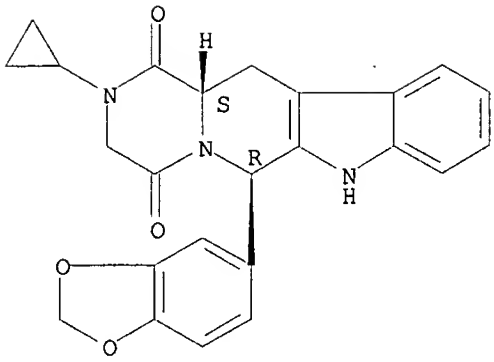

RN 171488-14-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



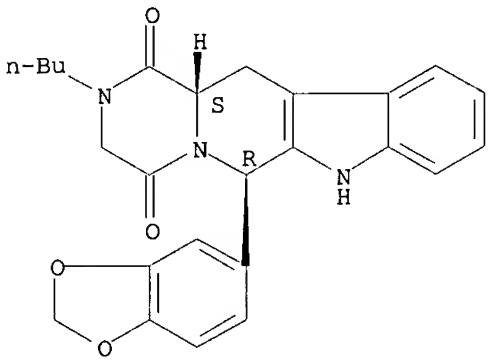

RN 171488-15-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopropyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



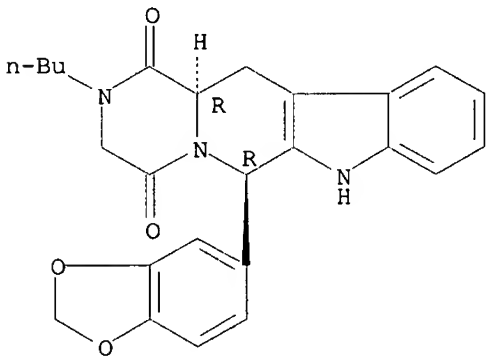
RN 171488-16-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-17-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

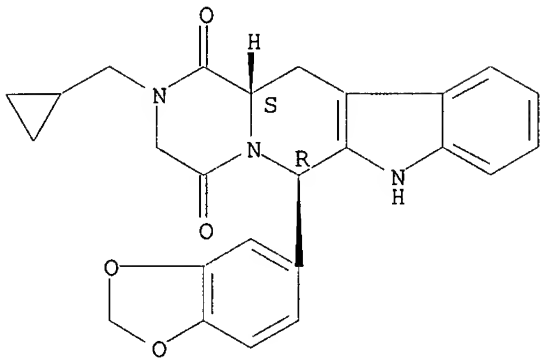
Relative stereochemistry.



RN 171488-18-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclopropylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA

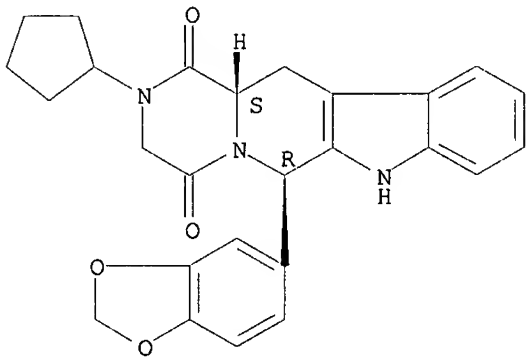
INDEX NAME)

Relative stereochemistry.



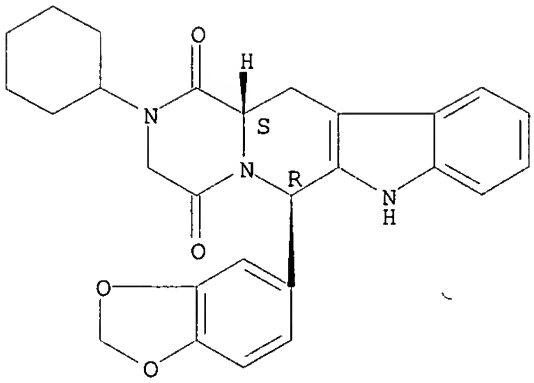
RN 171488-19-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



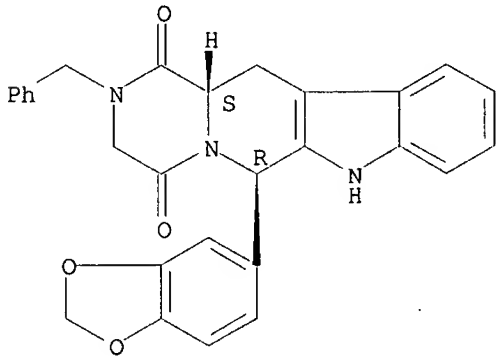
RN 171488-20-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclohexyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



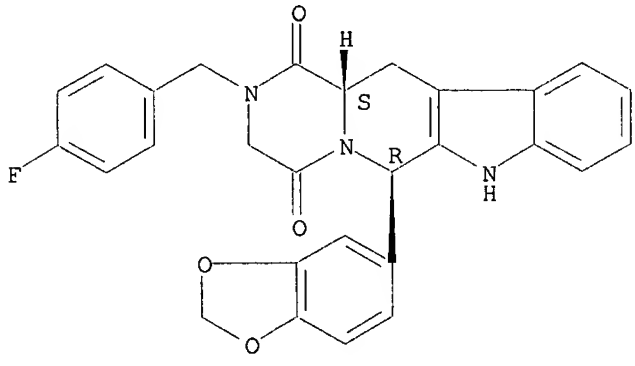
RN 171488-21-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(phenylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



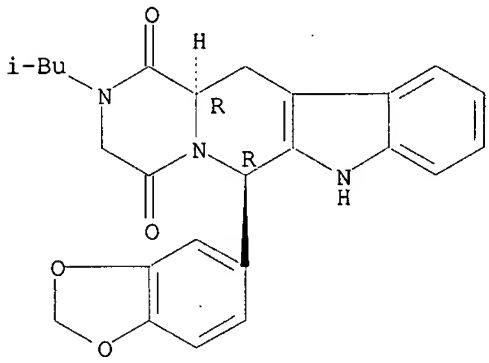
RN 171488-22-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(4-fluorophenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



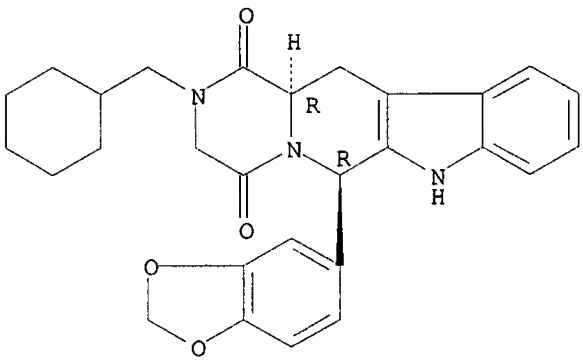
RN 171488-76-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-methylpropyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



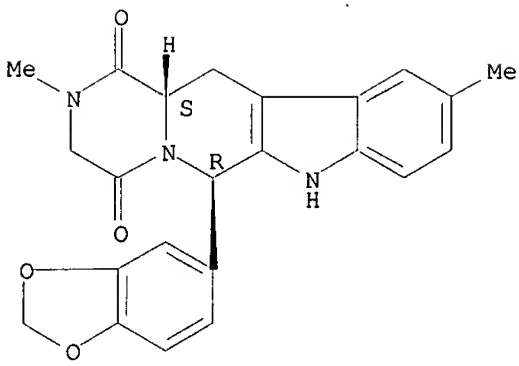
RN 171488-77-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclohexylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



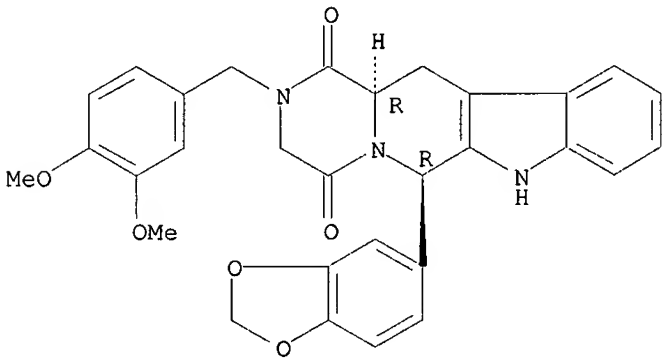
RN 171488-86-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,10-dimethyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



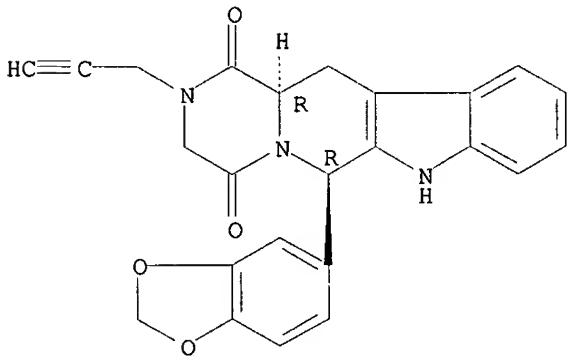
RN 171488-87-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(3,4-dimethoxyphenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171488-91-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-propynyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

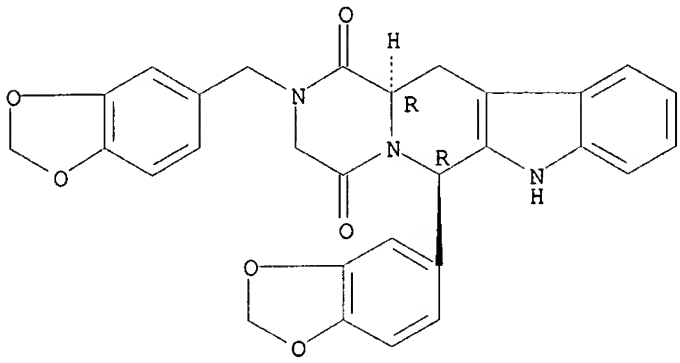
Absolute stereochemistry. Rotation (+).



RN 171488-92-9 CAPLUS

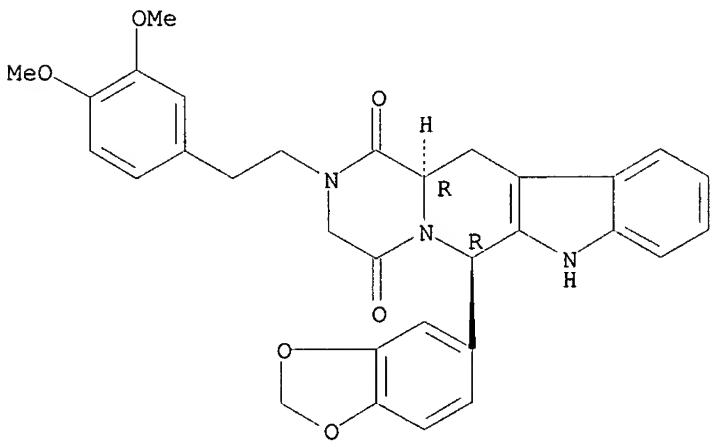
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(1,3-benzodioxol-5-ylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



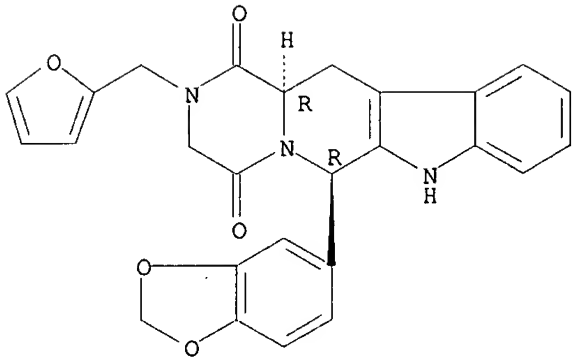
RN 171488-93-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(3,4-dimethoxyphenyl)ethyl]-2,3,6,7,12,12a-hexahydro-, (6R-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



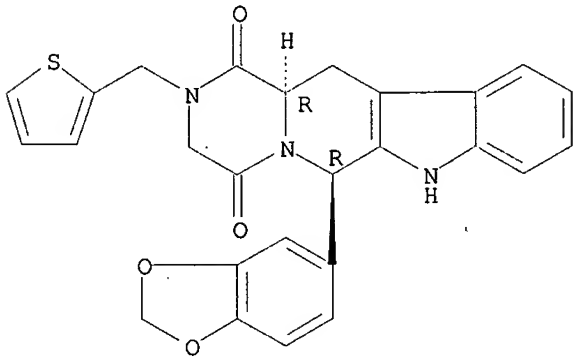
RN 171488-94-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(2-furanylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



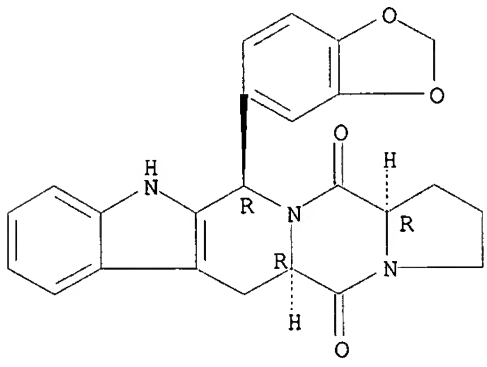
RN 171488-95-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-thienylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171489-01-3 CAPLUS
CN 5H,14H-Pyrrolo[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-5,14-dione, 12-(1,3-benzodioxol-5-yl)-1,2,3,5a,6,11,12,14a-octahydro-, (5aR,12R,14aR)- (9CI) (CA INDEX NAME)

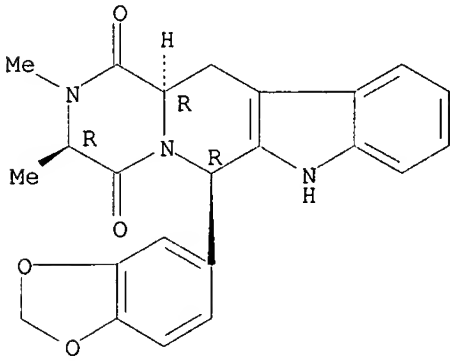
Absolute stereochemistry. Rotation (+).



RN 171489-02-4 CAPLUS

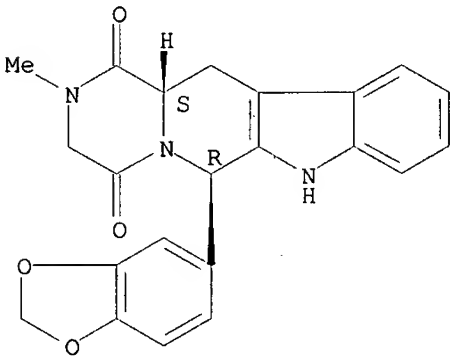
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



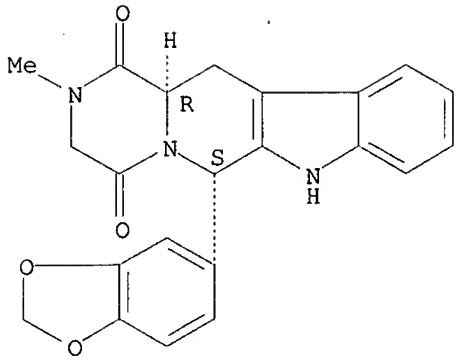
RN 171596-27-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



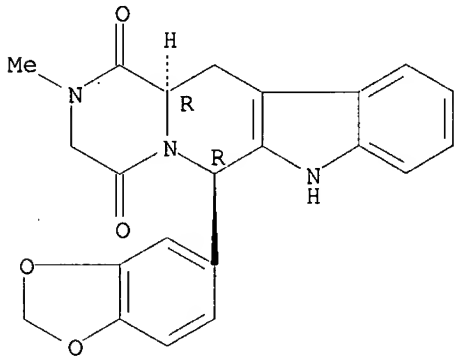
RN 171596-28-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6S,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



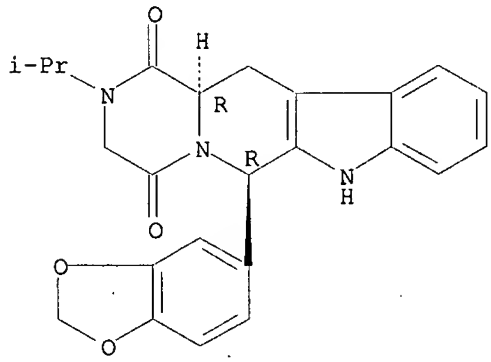
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-30-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

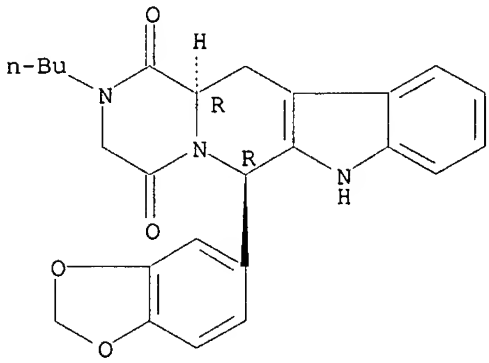
Absolute stereochemistry. Rotation (+).



RN 171596-31-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-

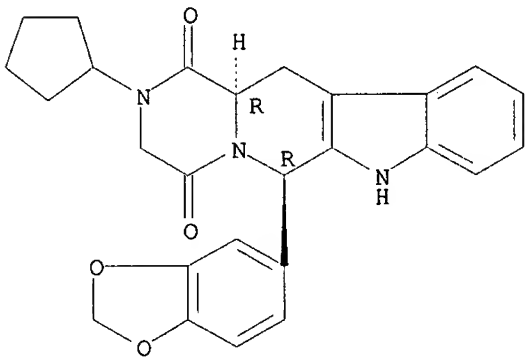
2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



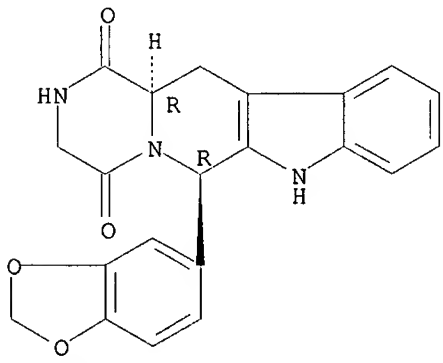
RN 171596-32-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



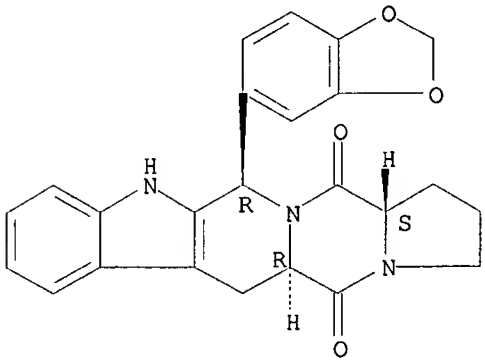
RN 171596-36-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



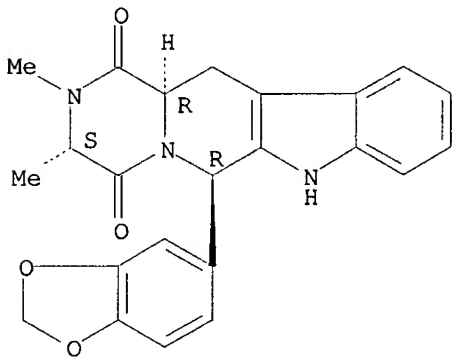
RN 171596-39-7 CAPLUS
CN 5H,14H-Pyrrolo[1'',2'':4',5']pyrazino[1',2':1,6]pyrido[3,4-b]indole-5,14-dione, 12-(1,3-benzodioxol-5-yl)-1,2,3,5a,6,11,12,14a-octahydro-, (5aR,12R,14aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s e1
L3            1 171596-29-5/BI
                (171596-29-5/RN)

=> d ide

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RN   171596-29-5  REGISTRY
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     2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI)  (CA INDEX NAME)
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OTHER NAMES:
CN   Cialis
CN   GF 196960
CN   IC 351
CN   ICOS 351
CN   Tadalafil
FS   STEREOSEARCH
DR   240822-07-5, 282541-36-0
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       USPAT2, USPATFULL

Absolute stereochemistry.  Rotation (+).
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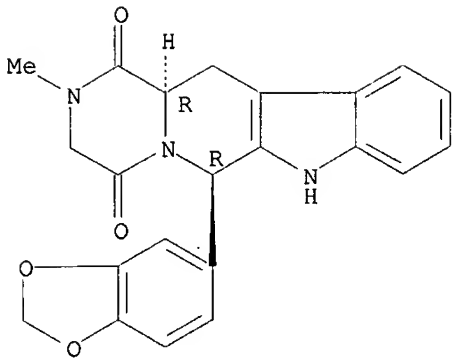

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

32 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
32 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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L4 1 171596-40-0/BI
(171596-40-0/RN)

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L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **171596-40-0** REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
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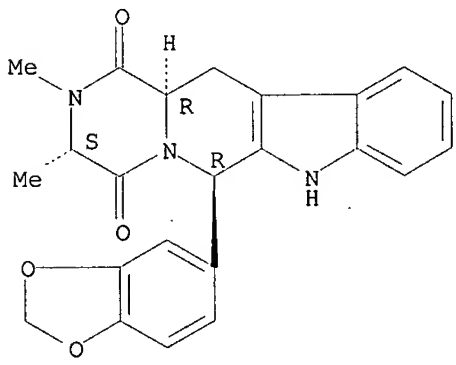
Absolute stereochemistry. Rotation (+).



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8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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L5 1 304683-09-8/BI
(304683-09-8/RN)

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L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **304683-09-8** REGISTRY
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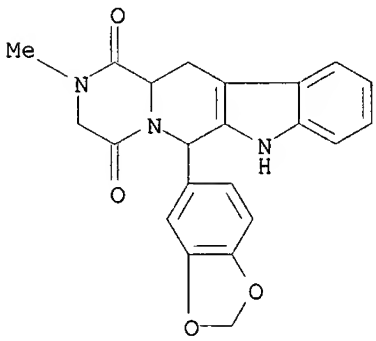
FS 3D CONCORD
MF C22 H19 N3 O4
SR CA
LC STN Files: CA, CAPLUS, DRUGPAT, DRUGUPDATES



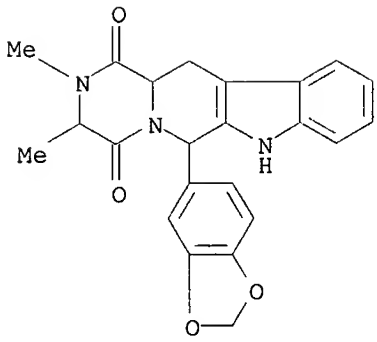

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s e4
L6 1 304683-11-2/BI
(304683-11-2/RN)

=> d ide

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **304683-11-2** REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H21 N3 O4
SR CA
LC STN Files: CA, CAPLUS



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s e5
L7 1 9068-52-4/BI
(9068-52-4/RN)

=> d ide

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **9068-52-4** REGISTRY
CN Phosphodiesterase, guanosine cyclic 3',5'-phosphate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3',5'-cGMP phosphodiesterase
CN 3',5'-Cyclic GMP phosphodiesterase
CN cGMP phosphodiesterase
CN cGMP-binding cGMP-specific phosphodiesterase
CN cGMP-dependent phosphodiesterase
CN cGMP-specific cyclic nucleotide phosphodiesterase
CN cGMP-specific phosphodiesterase
CN Cyclic 3',5'-GMP phosphodiesterase
CN Cyclic GMP phosphodiesterase
CN Cyclic GMP-dependent phosphodiesterase
CN Cyclic guanosine 3',5'-monophosphate phosphodiesterase
CN Cyclic guanosine 3',5'-phosphate phosphodiesterase
CN E.C. 3.1.4.35
CN Guanosine cyclic 3',5'-phosphate phosphodiesterase
CN Guanylate phosphodiesterase
CN Phosphodiesterase 6
CN Phosphodiesterase type 5
CN Phosphodiesterase V
CN Phosphodiesterase VI
CN Photoreceptor phosphodiesterase
CN Type V cGMP-specific phosphodiesterase
CN Type V phosphodiesterase
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CIN, EMBASE, IFICDB, IFIPAT, IFIUDB, PROMT, TOXCENTER, USPAT2, USPATFULL

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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            1856 REFERENCES IN FILE CA (1967 TO DATE)
               7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1867 REFERENCES IN FILE CAPLUS (1967 TO DATE)


=> file embase; d que l18
FILE 'EMBASE' ENTERED AT 14:58:53 ON 16 JUL 2002
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 FILE COVERS 1974 TO 11 Jul 2002 (20020711/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L17           25 SEA FILE=EMBASE ABB=ON  PLU=ON  TARDANAFIL/CT
L18            9 SEA FILE=EMBASE ABB=ON  PLU=ON  L17/MAJ


=> file wpid; d que l19
FILE 'WPIDS' ENTERED AT 14:59:16 ON 16 JUL 2002
COPYRIGHT (C) 2002 THOMSON DERWENT

FILE LAST UPDATED: 11 JUL 2002              <20020711/UP>
MOST RECENT DERWENT UPDATE            200244   <200244/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L19            9 SEA FILE=WPIDS ABB=ON  PLU=ON  CIALIS OR TADALAFIL OR TARDANAFI
                 L OR IC351 OR (IC OR ICOS) (W) 351


=> file biosis; d que l21
FILE 'BIOSIS' ENTERED AT 15:02:48 ON 16 JUL 2002
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 10 July 2002 (20020710/ED)
```

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L21          16 SEA FILE=BIOSIS ABB=ON  PLU=ON  CIALIS OR IC351 OR (IC OR
                ICOS) (W) (351) OR TADALAFIL OR TARDANAFIL OR GF196960 OR GF
                (W) (196960 OR 196 960)


=> file medline; d que l23
FILE 'MEDLINE' ENTERED AT 15:02:56 ON 16 JUL 2002

 FILE LAST UPDATED: 13 JUL 2002 (20020713/UP). FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.


L23           6 SEA FILE=MEDLINE ABB=ON  PLU=ON  IC351


=> dup rem l12 l23 l19 l21 l23
FILE 'CAPLUS' ENTERED AT 15:04:37 ON 16 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 15:04:37 ON 16 JUL 2002

FILE 'WPIDS' ENTERED AT 15:04:37 ON 16 JUL 2002
COPYRIGHT (C) 2002 THOMSON DERWENT

FILE 'BIOSIS' ENTERED AT 15:04:37 ON 16 JUL 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)
PROCESSING COMPLETED FOR L12
PROCESSING COMPLETED FOR L23
PROCESSING COMPLETED FOR L19
PROCESSING COMPLETED FOR L21
L25           58 DUP REM L12 L23 L19 L21 L23 (10 DUPLICATES REMOVED)
                 ANSWERS '1-37' FROM FILE CAPLUS - Answers 1-37 previously displayed in
                 ANSWERS '38-43' FROM FILE MEDLINE structure search
                 ANSWER '44' FROM FILE WPIDS
                 ANSWERS '45-58' FROM FILE BIOSIS

=> d ibib ab l25 38-58

L25  ANSWER 38 OF 58     MEDLINE                          DUPLICATE 6
ACCESSION NUMBER:    2001335647     MEDLINE
DOCUMENT NUMBER:     21296319   PubMed ID: 11402584
TITLE:               Oral drug therapy for erectile dysfunction.
AUTHOR:              Padma-Nathan H; Giuliano F
CORPORATE SOURCE:    Department of Urology, Keck School of Medicine, University
                     of Southern California Beverly Hills, California, USA.
SOURCE:              UROLOGIC CLINICS OF NORTH AMERICA, (2001 May) 28 (2)
                     321-34.  Ref: 39
                     Journal code: 0423221. ISSN: 0094-0143.
PUB. COUNTRY:        United States
                     Journal; Article; (JOURNAL ARTICLE)
```

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB Oral drugs are a well-established, first-line therapy for erectile dysfunction. As a result of the success of sildenafil, a plethora of new drugs for erectile dysfunction are on the horizon. Apomorphine and **IC351** are in late phase III development. Vardenafil (Bayer, New Haven, CT), a PDE5 inhibitor, and the combination of yohimbine and L-arginine (NitroMed, Boston, MA) are in early phase III development. Early clinical and preclinical studies are investigating new phosphodiesterase inhibitors, cyclic AMP activators, alpha-adrenergic antagonists, dopamine agonists, melanocyte-stimulating hormone, potassium channel modulators, endothelin antagonists, and new nitric oxide donors. The future is bright for this infant field of sexual pharmacotherapy.

L25 ANSWER 39 OF 58 MEDLINE
ACCESSION NUMBER: 2002117405 MEDLINE
DOCUMENT NUMBER: 21838816 PubMed ID: 11850737
TITLE: **IC351** (tadalafil, Cialis): update on clinical experience.
AUTHOR: Porst H
CORPORATE SOURCE: Urological practice, Hamburg, Germany.. Porst20354@aol.com
SOURCE: INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH, (2002 Feb) 14 Suppl 1 S57-64. Ref: 12
Journal code: 9007383. ISSN: 0955-9930.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020220
Last Updated on STN: 20020613
Entered Medline: 20020612

AB **IC351** (tadalafil, trade name Cialis) is a new representative compound of the second generation of selective phosphodiesterase 5 (PDE-5) inhibitors. The selectivity ratio vs PDE-5 is more than 10 000 for PDE-1 through PDE-4 and PDE-7 through PDE-10 and 780 for PDE-6. In the European daily-dosing trial, the efficacy rates were up to 93% for successful intercourses with completion in the 50-mg dose in patients with mild to moderate erectile dysfunction (ED). In two different dose-ranging studies with 2-25 mg taken as needed, efficacy rates of up to 88% improvement in erections and up to 73% successful intercourses with completion were achieved. In a placebo-controlled, fixed-dose (10- and 20-mg) trial in diabetic patients, improved erections of 56% and 64% were reported compared with 25% after placebo. Drug-related adverse effects, with headache in up to 23% of patients (placebo, up to 17%), dyspepsia in up to 11% (placebo, up to 7%), back pain in up to 4.7% (placebo, 0%), and myalgia in up to 4.1% (placebo, up to 2.4%), were mostly mild to moderate. Neither drug-related serious cardiovascular adverse events nor color vision disturbances were encountered. The long half-life (>17 h), with a comfortably long window of opportunity, releases couples from the need to plan sexual activities and therefore provides the highest amount of spontaneity for sexual activities.

L25 ANSWER 40 OF 58 MEDLINE
ACCESSION NUMBER: 2002073964 MEDLINE
DOCUMENT NUMBER: 21658223 PubMed ID: 11799971
TITLE: Towards optimal ED management: educational forum - II.
AUTHOR: Brock G
CORPORATE SOURCE: Division of Urology, Department of Surgery, University of Western Ontario, London, Ontario.
SOURCE: Can J Urol, (2001 Dec) 8 (6) 1419-20.
Journal code: 9515842. ISSN: 1195-9479.
PUB. COUNTRY: Canada
Conference; Conference Article; (CONGRESSES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020206
Entered Medline: 20020205

L25 ANSWER 41 OF 58 MEDLINE
ACCESSION NUMBER: 2001342867 MEDLINE
DOCUMENT NUMBER: 21298873 PubMed ID: 11406522
TITLE: Importance of NF-kappaB in rheumatoid synovial tissues: in situ NF-kappaB expression and in vitro study using cultured synovial cells.
AUTHOR: Yamasaki S; Kawakami A; Nakashima T; Nakamura H; Kamachi M; Honda S; Hirai Y; Hida A; Ida H; Migita K; Kawabe Y; Koji T; Furuichi I; Aoyagi T; Eguchi K
CORPORATE SOURCE: The First Department of Internal Medicine, Nagasaki University School of Medicine, 1-7-1 Sakamoto, Nagasaki, Japan.
SOURCE: ANNALS OF THE RHEUMATIC DISEASES, (2001 Jul) 60 (7) 678-84.
Journal code: 0372355. ISSN: 0003-4967.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010716
Last Updated on STN: 20010716
Entered Medline: 20010712

AB OBJECTIVES: To examine whether inhibition of NF-kappaB induces apoptosis of human synovial cells stimulated by tumour necrosis factor alpha (TNFalpha), interleukin 1beta (IL1beta), and anti-Fas monoclonal antibody (mAb). METHODS: The expression of proliferating cell nuclear antigen (PCNA), NF-kappaB, and the presence of apoptotic synovial cells were determined in synovial tissues. Apoptosis of cultured synovial cells was induced by inhibition of NF-kappaB nuclear translocation by Z-Leu-Leu-Leu-aldehyde (LLL-CHO). The activation of caspase-3 and expression of XIAP and cIAP2 in synovial cells in LLL-CHO induced apoptosis was also examined. RESULTS: Abundant PCNA+ synovial cells were found in rheumatoid arthritis (RA) synovial tissue, though a few apoptotic synovial cells were also detected in the RA synovial tissues. Nuclear NF-kappaB was expressed in RA synovial cells. Electrophoretic mobility shift assay showed that treatment of cells with TNFalpha or IL1beta significantly stimulated nuclear NF-kappaB activity. A small number of apoptotic synovial cells expressing intracellular active caspase-3 were found after treatment of cells with LLL-CHO. Although treatment of RA synovial cells with TNFalpha or IL1beta alone did not induce apoptosis, apoptosis induced by LLL-CHO and caspase-3 activation were clearly enhanced in TNFalpha or IL1beta stimulated synovial cells compared with unstimulated synovial cells. Furthermore, induction of apoptosis of

synovial cells with caspase-3 activation by anti-Fas mAb was clearly increased by LLL-CHO. The expression of cIAP2 and XIAP in synovial cells may not directly influence the sensitivity of synovial cells to apoptosis induced by LLL-CHO. CONCLUSION: The results suggest that NF-kappaB inhibition may be a potentially important therapeutic approach for RA by correcting the imbalance between apoptosis and proliferation of synovial cells in RA synovial tissue.

L25 ANSWER 42 OF 58 MEDLINE
ACCESSION NUMBER: 2001382350 MEDLINE
DOCUMENT NUMBER: 21213761 PubMed ID: 11313831
TITLE: On-demand **IC351** (Cialis) enhances erectile function in patients with erectile dysfunction.
AUTHOR: Padma-Nathan H; McMurray J G; Pullman W E; Whitaker J S; Saoud J B; Ferguson K M; Rosen R C
CORPORATE SOURCE: Keck School of Medicine, University of Southern California, Los Angeles, California 90212, USA. (IC351 On-Demand Dosing Study Group).
SOURCE: INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH, (2001 Feb) 13 (1) 2-9.
Journal code: 9007383. ISSN: 0955-9930.
PUB. COUNTRY: England: United Kingdom
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705
AB **IC351** (Cialis) is a selective inhibitor of PDE5. The efficacy and safety of on-demand dosing of **IC351** in men with erectile dysfunction was assessed in a multicenter, double-blind, placebo-controlled study. One hundred seventy-nine men (mean age: 56 y) were randomized to receive placebo or **IC351** at doses of 2, 5, 10 or 25 mg, taken on demand over a 3-week period. The primary endpoints were change from baseline in responses to Questions 3 (Q3) and 4 (Q4) of the International Index of Erectile Function (IIEF). **IC351** significantly improved IIEF Q3 scores at all doses vs placebo (P < or =0.003). **IC351** also significantly improved IIEF Q4 scores in all but the 2 mg group (P < or =0.0003). No significant changes in laboratory values, ECGs, or blood pressure were observed. The most common adverse events were headache and dyspepsia. The conclusion of this study was that on-demand **IC351** at doses up to 25 mg was well tolerated and significantly improved erectile function.

L25 ANSWER 43 OF 58 MEDLINE
ACCESSION NUMBER: 2002005986 MEDLINE
DOCUMENT NUMBER: 21064306 PubMed ID: 11122955
TITLE: Recent developments in male sexual dysfunction.
AUTHOR: Shabsigh R
CORPORATE SOURCE: Department of Urology, Columbia-Presbyterian Medical Center, 161 Fort Washington Avenue, New York, NY 10032, USA.. rs66@columbia.edu
SOURCE: Curr Psychiatry Rep, (2000 Jun) 2 (3) 196-200. Ref: 8
Journal code: 100888960. ISSN: 1523-3812.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020501
Entered Medline: 20020430

AB The past few years have witnessed major developments in the management of male sexual dysfunction. The introduction of the first efficacious and safe oral medication (sildenafil) resulted in the expansion of the patient base and, the change in health care delivery, with erectile dysfunction (ED) entering the primary care physician's practice. New guidelines for the diagnosis and treatment of ED have been developed, including the Process of Care in the USA and the 1st International Consultation on ED sponsored by the World Health Organization. Well-defined algorithms for diagnosis and treatment have been adopted. These recent developments have brought up challenging issues, including the cardiovascular safety of sexual activity, societal changes, internet prescriptions, definition of the patient, expansion of clinical and laboratory research, rise of interest in female sexual dysfunction, and a significant economic impact. The recent developments in male sexual dysfunction continue with the study of new oral medications. Some of these new medications, such as sublingual apomorphine, have a central mode of action, whereas others, such as the phosphodiesterase inhibitor **IC351**, have a selective peripheral vasodilation-enhancing action.

L25 ANSWER 44 OF 58 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-572170 [53] WPIDS
DOC. NO. CPI: C2000-170623
TITLE: New nitrosated and nitrosylated prostaglandins, useful for treating or preventing e.g. sexual dysfunction in males and females, cerebrovascular disorders and glaucoma.
DERWENT CLASS: B05
INVENTOR(S): GARVEY, D S; GASTON, R D; LETTS, G L; SAENZ DE TEJADA, I; TAM, S W; WORCEL, M
PATENT ASSIGNEE(S): (NITR-N) NITROMED INC
COUNTRY COUNT: 90
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2000051978 | A1 | 20000908 | (200053)* | EN | 82 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW | | | | | |
| W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW | | | | | |
| AU 2000037136 | A | 20000921 | (200065) | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2000051978 | A1 | WO 2000-US5286 | 20000301 |
| AU 2000037136 | A | AU 2000-37136 | 20000301 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|

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AU 2000037136 A Based on WO 200051978

PRIORITY APPLN. INFO: US 1999-138502P 19990609; US 1999-122273P 19990301

AB WO 200051978 A UPAB: 20001023

NOVELTY - Nitrosated and nitrosylated prostaglandins (I) and compositions comprising them are new, also compositions comprising a prostaglandin and S-nitrosothiol compound.

DETAILED DESCRIPTION - Nitrosated and nitrosylated prostaglandins of formula (I) are new:

bonds a', b', c', d' = single or double bonds;

R1 = -OD1 or Cl;

R2, R8 = H; or

R1+R2 = =CH2 or =O;

R3, R4 = H, -OD1 or Me;

R5, R6 = H, -OD1, Me, OMe or -CH=CH2;

R7 = H or OD1;

R9 = H or absent when the C to which it is attached is the central carbon of an allene; or

R8+R9+attached chain atoms = a substituted benzene ring provided that R1 is O which is attached to the C at the position of the benzene ring defined by B';

A = -CH=, -CH2-, -S- or -O-;

B' = -CH=, -CH2-, -S- or -C(O)-;

X = -CH2OR11, -C(O)OR11 or -C(O)N(D1)R12;

R11 = D1, 1-10C alkyl or a group of formula (i):

R12 = -S(O)2CH3 or -C(O)CH3;

Z' = ethyl, butyl, hexyl, benzyl, -CH2-O-CH2-CH3, -CH(CH3)-(CH2)3-CH3 or a group of formula (ii) or (iii):

R13 = H or Cl;

D1 = H or D; provided that at least 1 D1 is D;

D = Q or K;

Q = -NO or NO2;

K = -Wa-Eb-(C(Re)(Rf))p-Ec-(C(Re)(Rf))x-Wd -(C(Re)(Rf))y-Wi-Ej-Wg-(C(Re)(Rf))z-T-Q;

a, b, c, d, g, i, j = 0-3;

p, x, y, z = 0-10;

E = -T-, alkyl, aryl, (C(Re)(Rf))h-,

W = -C(O)-, -C(S)- or as defined for E;

h = 1 10;

q = 1-5;

Re, Rf = H, alkyl, cycloalkoxy, halo, OH, hydroxyalkyl, alkoxyalkyl, aryl-heterocyclic, alkylaryl, cycloalkylalkyl, heterocyclic-alkyl, alkoxy, haloalkoxy, NH2, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkoxyhaloalkyl, haloalkoxy, sulfonic acid, sulfonic ester, alkylsulfonic acid, arylsulfonic acid, arylalkoxy, alkylthio, arylthio, cycloalkylthio, cycloalkenyl, CN, aminoalkyl, aminoaryl, aryl, arylalkyl, alkylaryl, carboxamido, alkylcarboxamido, arylcarboxamido, amidyl, carboxyl, carbamoyl, alkylcarboxylic acid, arylcarboxylic acid, alkylcarbonyl, arylcarbonyl, ester, carboxylic ester, alkylcarboxylic ester, arylcarboxylic ester, haloalkoxy, sulfonamido, alkylsulfonamido, arylsulfonamido, sulfonic ester, a urea, phosphoryl, nitro, -T-Q or -(C(Re)(Rf))k-T-Q; or

Re+Rf+attached C atoms = carbonyl, methanthial, heterocyclic, cycloalkyl or a bridged cycloalkyl;

k = 1-3;

T = a covalent bond, carbonyl, O, -S(O)o- or -N(Ra)Ri-;

o = 0-2;

Ra = a lone pair of electrons, H or alkyl;

Ri = H, alkyl, aryl, alkylcarboxylic acid, arylcarboxylic acid,

alkylcarboxylic ester, arylcarboxylic ester, alkylcarboxamido, arylcarboxamido, alkylaryl, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, sulfonamido, carboxamido, carboxylic ester, amino alkyl, amino aryl, -CH2-C(T-Q)(Re)(Rf) or -(N2O2)-M+;

M+ = an organic or inorganic cation;

provided that when Ri is -CH2-C(T-Q)(Re)(Rf) or -(N2O2) M+; or Re or Rf are T-Q or (C(Re)(Rf))k-T-Q, then T-Q can be H, alkyl, alkoxy, alkoxyalkyl, aminoalkyl, OH, heterocyclic or aryl; and provided that when X is -C(O)OD1 and D1 is K, then K is not alkyl or cycloalkyl mononitrate; benzoic acid substituted benzyloxy mononitrate; ethylene glycol mononitrate; polyethylene glycol mononitrate; the regioisomeric esters of glycerol dinitrate and oligomers as disclosed in WO9858910.

INDEPENDENT CLAIMS are included for the following:

(a) compositions and kits comprising (I) and at least 1 compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase, and/or at least 1 vasoactive agent; and

(b) compositions and kits comprising at least 1 prostaglandin and at least 1 S-nitrosothiol compound, useful for treating sexual dysfunction, a cerebrovascular disorder, cardiovascular disorder, benign prostatic hyperplasia, organ transplants, glaucoma or peptic ulcer, or for inducing an abortion.

ACTIVITY - Vasotropic; Cerebroprotective; Cardiant; Cytostatic; Ophthalmological; Antiulcer; Gynecological; Relaxant.

MECHANISM OF ACTION - Smooth muscle relaxant; Nitric oxide donor; Endothelium-derived relaxing factor agonist.

USE - For treating or preventing sexual dysfunction in males or females, treating a cerebrovascular disorder, cardiovascular disorder, benign prostatic hyperplasia, organ transplants, glaucoma or peptic ulcer, or for inducing an abortion (all claimed).

ADVANTAGE - The combination of a prostaglandin and a S-nitrosothiol gives synergistic results.

Dwg.0/4

L25 ANSWER 45 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:355438 BIOSIS
DOCUMENT NUMBER: PREV200200355438
TITLE: Efficacy and safety of **tadalafil** in men with erectile dysfunction with and without hypertension.
AUTHOR(S): Padma-Nathan, H. (1); Brock, G.; McMahon, C.; Chen, K. K.; Anglin, G.; Costigan, T.; Shen, W.; Watkins, V.; Whitaker, J. S.
CORPORATE SOURCE: (1) Keck School of Medicine, University of Southern California, Beverly Hills, CA USA
SOURCE: American Journal of Hypertension, (April, 2002) Vol. 15, No. 4 Part 2, pp. 143A-144A. http://www.ajh-us.org. print. Meeting Info.: Seventeenth Annual Scientific Meeting of the American Society of Hypertension New York, N.Y., USA May 14-18, 2002
ISSN: 0895-7061.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 46 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:355428 BIOSIS
DOCUMENT NUMBER: PREV200200355428
TITLE: Blood pressure and cardiovascular effects of **tadalafil**, a new PDE5 inhibitor.
AUTHOR(S): Hutter, A. M. (1); Kloner, R. A.; Watkins, V.; Costigan, T.; Bedding, A.; Mitchell, M.; Emmick, J.

CORPORATE SOURCE: (1) Massachusetts General Hospital, Harvard Medical School, Boston, MA USA
SOURCE: American Journal of Hypertension, (April, 2002) Vol. 15, No. 4 Part 2, pp. 140A. http://www.ajh-us.org. print.
Meeting Info.: Seventeenth Annual Scientific Meeting of the American Society of Hypertension New York, N.Y., USA May 14-18, 2002
ISSN: 0895-7061.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 47 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:449004 BIOSIS
DOCUMENT NUMBER: PREV200100449004
TITLE: CialisTM (**IC351**) as a treatment of erectile dysfunction in diabetic men.
AUTHOR(S): Saenz De Tejada, Inigo (1); Fredlund, Paul (1); Anglin, Greg (1); Pullman, Bill (1); Emmick, Jeff (1)
CORPORATE SOURCE: (1) Madrid Spain
SOURCE: Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A425. print.
Meeting Info.: 61st Scientific Sessions of the American Diabetes Association Philadelphia, Pennsylvania, USA June 22-26, 2001
ISSN: 0012-1797.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 48 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:380171 BIOSIS
DOCUMENT NUMBER: PREV200100380171
TITLE: CialisTM (**IC351**) provides prompt response and extended period of responsiveness for the treatment of men with erectile dysfunction (ED.
AUTHOR(S): Padma-Nathan, Harin (1); Rosen, Raymond C.; Shabsigh, Ridwan; Saikali, Khalil; Watkins, Vish S.; Pullman, Bill
CORPORATE SOURCE: (1) Los Angeles, CA USA
SOURCE: Journal of Urology, (May, 2001) Vol. 165, No. 5 Supplement, pp. 224. print.
Meeting Info.: Annual Meeting of the American Urological Association, Inc. Anaheim, California, USA June 02-07, 2001
ISSN: 0022-5347.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 49 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:381536 BIOSIS
DOCUMENT NUMBER: PREV200100381536
TITLE: Cellular localisation of phosphodiesterase type 11 (PDE11) in human corpus cavernosum and the contribution of PDE11 inhibition on nerve-stimulated relaxation.
AUTHOR(S): Baxendale, Rhona W. (1); Wayman, Christopher P. (1); Turner, Leigh (1); Phillips, Stephen C. (1)
CORPORATE SOURCE: (1) Sandwich UK
SOURCE: Journal of Urology, (May, 2001) Vol. 165, No. 5 Supplement, pp. 223-224. print.
Meeting Info.: Annual Meeting of the American Urological Association, Inc. Anaheim, California, USA June 02-07, 2001
ISSN: 0022-5347.

DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 50 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:262700 BIOSIS
DOCUMENT NUMBER: PREV200100262700
TITLE: CialisTM (**IC351**): Effective and well-tolerated treatment for ED.
AUTHOR(S): Brock, G. (1); Iglesias, J.; Toulouse, K.; Ferguson, K.; Pullman, W.; Anglin, G.
CORPORATE SOURCE: (1) Univ W Ontario, London, ON Canada
SOURCE: Journal of Andrology, (May June, 2001) No. Supplement, pp. 185. print.
Meeting Info.: VIIth International Congress of Andrology Montreal, Canada June 15-19, 2001
ISSN: 0196-3635.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 51 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:389604 BIOSIS
DOCUMENT NUMBER: PREV200100389604
TITLE: Efficacy and safety of **IC351** treatment for ED.
AUTHOR(S): Brock, G. (1); Iglesias, J.; Toulouse, K.; Ferguson, K.; Pullman, W.; Anglin, G.
CORPORATE SOURCE: (1) Univ. of W. Ontario, London, ON Canada
SOURCE: European Urology, (March, 2001) Vol. 39, No. Suppl. 5, pp. 106. print.
Meeting Info.: XVIth Congress of the European Association of Urology Geneva, Switzerland April 07-10, 2001
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 52 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:391998 BIOSIS
DOCUMENT NUMBER: PREV200100391998
TITLE: **IC351** enhances NO-mediated relaxation of human arterial and trabecular penile smooth muscle.
AUTHOR(S): Angulo, J. (1); Gadau, M.; Fernandez, A.; Gabancho, S.; Cuevas, P.; Martins, T.; Florio, V.; Ferguson, K.; Saenz De Tejada, I.
CORPORATE SOURCE: (1) Hospital Ramon y Cajal, Madrid Spain
SOURCE: European Urology, (March, 2001) Vol. 39, No. Suppl. 5, pp. 106. print.
Meeting Info.: XVIth Congress of the European Association of Urology Geneva, Switzerland April 07-10, 2001
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 53 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:375151 BIOSIS
DOCUMENT NUMBER: PREV200100375151
TITLE: The effect of on-demand **IC351** treatment of erectile dysfunction in men with diabetes.
AUTHOR(S): Saenz De Tejada, Inigo (1); Emmick, J.; Anglin, G.;

Fredlund, P.; Pullman, W.
CORPORATE SOURCE: (1) Hospital Ramon y Cajal, Madrid Spain
SOURCE: European Urology, (March, 2001) Vol. 39, No. Suppl. 5, pp. 16. print.
Meeting Info.: XVIth Congress of the European Association of Urology Geneva, Switzerland April 07-10, 2001
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 54 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:211709 BIOSIS
DOCUMENT NUMBER: PREV200000211709
TITLE: Daily and on-demand **IC351** treatment of erectile dysfunction.
AUTHOR(S): Giuliano, Francois (1); Porst, Hartmut; Padma-Nathan, Harin; Saoud, Jay; Ferguson, Kenneth; Whitaker, Steven; Pullman, William; Rosen, Raymond
CORPORATE SOURCE: (1) Bicetre France
SOURCE: Journal of Urology, (April, 2000) Vol. 163, No. 4 Suppl., pp. 201.
Meeting Info.: 95th Annual Meeting of the American Urological Association, Inc. Atlanta, Georgia, USA April 29, 2000-May 04, 1999
ISSN: 0022-5347.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 55 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:356087 BIOSIS
DOCUMENT NUMBER: PREV200000356087
TITLE: On-demand treatment of erectile dysfunction with **IC351**.
AUTHOR(S): Padma-Nathan, Harin (1); McMurray, James; Saoud, Jay; Ferguson, Kenneth; Pullman, William; Whitaker, Steven; Rosen, Raymond
CORPORATE SOURCE: (1) Male Clinic, University of Southern California, Santa Monica, CA USA
SOURCE: European Urology, (March, 2000) Vol. 37, No. Suppl. 2, pp. 80. print.
Meeting Info.: XVth Congress of the European Association of Urology Brussels, Belgium April 12-15, 2000
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 56 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:356088 BIOSIS
DOCUMENT NUMBER: PREV200000356088
TITLE: Daily **IC351** treatment of erectile dysfunction.
AUTHOR(S): Giuliano, Francois (1); Meuleman, Eric; Saoud, Jay; Ferguson, Kenneth; Whitaker, Steven; Porst, Hartmut
CORPORATE SOURCE: (1) Department of Urology, University Hospital of Bicetre, Le Kremlin France
SOURCE: European Urology, (March, 2000) Vol. 37, No. Suppl. 2, pp. 80. print.
Meeting Info.: XVth Congress of the European Association of Urology Brussels, Belgium April 12-15, 2000

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L21          16 SEA FILE=BIOSIS ABB=ON  PLU=ON  CIALIS OR IC351 OR (IC OR
                ICOS) (W) (351) OR TADALAFIL OR TARDANAFIL OR GF196960 OR GF
                (W) (196960 OR 196 960)


=> file medline; d que l23
FILE 'MEDLINE' ENTERED AT 15:02:56 ON 16 JUL 2002

 FILE LAST UPDATED: 13 JUL 2002 (20020713/UP). FILE COVERS 1958 TO DATE.

 On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

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 SUBSTANCE IDENTIFICATION.

L23           6 SEA FILE=MEDLINE ABB=ON  PLU=ON  IC351


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PROCESSING COMPLETED FOR L21
L24          30 DUP REM L23 L19 L21 L23 (1 DUPLICATE REMOVED)
                ANSWERS '1-6' FROM FILE MEDLINE
                ANSWERS '7-15' FROM FILE WPIDS
                ANSWERS '16-30' FROM FILE BIOSIS

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PROCESSING COMPLETED FOR L23
PROCESSING COMPLETED FOR L19
PROCESSING COMPLETED FOR L21
L25          58 DUP REM L12 L23 L19 L21 L23 (10 DUPLICATES REMOVED)
                ANSWERS '1-37' FROM FILE CAPLUS
                ANSWERS '38-43' FROM FILE MEDLINE
                ANSWER '44' FROM FILE WPIDS
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ANSWERS '45-58' FROM FILE BIOSIS

=> d ibib ab l25 38-58

L25 ANSWER 38 OF 58 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001335647 MEDLINE
DOCUMENT NUMBER: 21296319 PubMed ID: 11402584
TITLE: Oral drug therapy for erectile dysfunction.
AUTHOR: Padma-Nathan H; Giuliano F
CORPORATE SOURCE: Department of Urology, Keck School of Medicine, University of Southern California Beverly Hills, California, USA.
SOURCE: UROLOGIC CLINICS OF NORTH AMERICA, (2001 May) 28 (2) 321-34. Ref: 39
Journal code: 0423221. ISSN: 0094-0143.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB Oral drugs are a well-established, first-line therapy for erectile dysfunction. As a result of the success of sildenafil, a plethora of new drugs for erectile dysfunction are on the horizon. Apomorphine and **IC351** are in late phase III development. Vardenafil (Bayer, New Haven, CT), a PDE5 inhibitor, and the combination of yohimbine and L-arginine (NitroMed, Boston, MA) are in early phase III development. Early clinical and preclinical studies are investigating new phosphodiesterase inhibitors, cyclic AMP activators, alpha-adrenergic antagonists, dopamine agonists, melanocyte-stimulating hormone, potassium channel modulators, endothelin antagonists, and new nitric oxide donors. The future is bright for this infant field of sexual pharmacotherapy.

L25 ANSWER 39 OF 58 MEDLINE
ACCESSION NUMBER: 2002117405 MEDLINE
DOCUMENT NUMBER: 21838816 PubMed ID: 11850737
TITLE: **IC351** (tadalafil, Cialis): update on clinical experience.
AUTHOR: Porst H
CORPORATE SOURCE: Urological practice, Hamburg, Germany.. Porst20354@aol.com
SOURCE: INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH, (2002 Feb) 14 Suppl 1 S57-64. Ref: 12
Journal code: 9007383. ISSN: 0955-9930.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020220
Last Updated on STN: 20020613
Entered Medline: 20020612

AB **IC351** (tadalafil, trade name Cialis) is a new representative compound of the second generation of selective phosphodiesterase 5 (PDE-5) inhibitors. The selectivity ratio vs PDE-5 is more than 10 000 for PDE-1 through PDE-4 and PDE-7 through PDE-10 and 780 for PDE-6. In the European daily-dosing trial, the efficacy rates were up to 93% for successful

intercourses with completion in the 50-mg dose in patients with mild to moderate erectile dysfunction (ED). In two different dose-ranging studies with 2-25 mg taken as needed, efficacy rates of up to 88% improvement in erections and up to 73% successful intercourses with completion were achieved. In a placebo-controlled, fixed-dose (10- and 20-mg) trial in diabetic patients, improved erections of 56% and 64% were reported compared with 25% after placebo. Drug-related adverse effects, with headache in up to 23% of patients (placebo, up to 17%), dyspepsia in up to 11% (placebo, up to 7%), back pain in up to 4.7% (placebo, 0%), and myalgia in up to 4.1% (placebo, up to 2.4%), were mostly mild to moderate. Neither drug-related serious cardiovascular adverse events nor color vision disturbances were encountered. The long half-life (>17 h), with a comfortably long window of opportunity, releases couples from the need to plan sexual activities and therefore provides the highest amount of spontaneity for sexual activities.

L25 ANSWER 40 OF 58 MEDLINE
ACCESSION NUMBER: 2002073964 MEDLINE
DOCUMENT NUMBER: 21658223 PubMed ID: 11799971
TITLE: Towards optimal ED management: educational forum - II.
AUTHOR: Brock G
CORPORATE SOURCE: Division of Urology, Department of Surgery, University of Western Ontario, London, Ontario.
SOURCE: Can J Urol, (2001 Dec) 8 (6) 1419-20.
Journal code: 9515842. ISSN: 1195-9479.
PUB. COUNTRY: Canada
Conference; Conference Article; (CONGRESSES)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020206
Entered Medline: 20020205

L25 ANSWER 41 OF 58 MEDLINE
ACCESSION NUMBER: 2001342867 MEDLINE
DOCUMENT NUMBER: 21298873 PubMed ID: 11406522
TITLE: Importance of NF-kappaB in rheumatoid synovial tissues: in situ NF-kappaB expression and in vitro study using cultured synovial cells.
AUTHOR: Yamasaki S; Kawakami A; Nakashima T; Nakamura H; Kamachi M; Honda S; Hirai Y; Hida A; Ida H; Migita K; Kawabe Y; Koji T; Furuichi I; Aoyagi T; Eguchi K
CORPORATE SOURCE: The First Department of Internal Medicine, Nagasaki University School of Medicine, 1-7-1 Sakamoto, Nagasaki, Japan.
SOURCE: ANNALS OF THE RHEUMATIC DISEASES, (2001 Jul) 60 (7) 678-84.
Journal code: 0372355. ISSN: 0003-4967.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010716
Last Updated on STN: 20010716
Entered Medline: 20010712
AB OBJECTIVES: To examine whether inhibition of NF-kappaB induces apoptosis of human synovial cells stimulated by tumour necrosis factor alpha (TNFalpha), interleukin 1beta (IL1beta), and anti-Fas monoclonal antibody (mAb). METHODS: The expression of proliferating cell nuclear antigen (PCNA), NF-kappaB, and the presence of apoptotic synovial cells were

determined in synovial tissues. Apoptosis of cultured synovial cells was induced by inhibition of NF-kappaB nuclear translocation by Z-Leu-Leu-Leu-aldehyde (LLL-CHO). The activation of caspase-3 and expression of XIAP and cIAP2 in synovial cells in LLL-CHO induced apoptosis was also examined. RESULTS: Abundant PCNA+ synovial cells were found in rheumatoid arthritis (RA) synovial tissue, though a few apoptotic synovial cells were also detected in the RA synovial tissues. Nuclear NF-kappaB was expressed in RA synovial cells. Electrophoretic mobility shift assay showed that treatment of cells with TNFalpha or IL1beta significantly stimulated nuclear NF-kappaB activity. A small number of apoptotic synovial cells expressing intracellular active caspase-3 were found after treatment of cells with LLL-CHO. Although treatment of RA synovial cells with TNFalpha or IL1beta alone did not induce apoptosis, apoptosis induced by LLL-CHO and caspase-3 activation were clearly enhanced in TNFalpha or IL1beta stimulated synovial cells compared with unstimulated synovial cells. Furthermore, induction of apoptosis of synovial cells with caspase-3 activation by anti-Fas mAb was clearly increased by LLL-CHO. The expression of cIAP2 and XIAP in synovial cells may not directly influence the sensitivity of synovial cells to apoptosis induced by LLL-CHO. CONCLUSION: The results suggest that NF-kappaB inhibition may be a potentially important therapeutic approach for RA by correcting the imbalance between apoptosis and proliferation of synovial cells in RA synovial tissue.

L25 ANSWER 42 OF 58 MEDLINE
ACCESSION NUMBER: 2001382350 MEDLINE
DOCUMENT NUMBER: 21213761 PubMed ID: 11313831
TITLE: On-demand **IC351** (Cialis) enhances erectile function in patients with erectile dysfunction.
AUTHOR: Padma-Nathan H; McMurray J G; Pullman W E; Whitaker J S; Saoud J B; Ferguson K M; Rosen R C
CORPORATE SOURCE: Keck School of Medicine, University of Southern California, Los Angeles, California 90212, USA. (IC351 On-Demand Dosing Study Group).
SOURCE: INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH, (2001 Feb) 13 (1) 2-9.
Journal code: 9007383. ISSN: 0955-9930.
PUB. COUNTRY: England: United Kingdom
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB **IC351** (Cialis) is a selective inhibitor of PDE5. The efficacy and safety of on-demand dosing of **IC351** in men with erectile dysfunction was assessed in a multicenter, double-blind, placebo-controlled study. One hundred seventy-nine men (mean age: 56 y) were randomized to receive placebo or **IC351** at doses of 2, 5, 10 or 25 mg, taken on demand over a 3-week period. The primary endpoints were change from baseline in responses to Questions 3 (Q3) and 4 (Q4) of the International Index of Erectile Function (IIEF). **IC351** significantly improved IIEF Q3 scores at all doses vs placebo (P < or =0.003). **IC351** also significantly improved IIEF Q4 scores in all but the 2 mg group (P < or =0.0003). No significant changes in laboratory values, ECGs, or blood pressure were observed. The most common adverse events were headache and dyspepsia. The conclusion of this study was that

on-demand **IC351** at doses up to 25 mg was well tolerated and significantly improved erectile function.

L25 ANSWER 43 OF 58 MEDLINE
ACCESSION NUMBER: 2002005986 MEDLINE
DOCUMENT NUMBER: 21064306 PubMed ID: 11122955
TITLE: Recent developments in male sexual dysfunction.
AUTHOR: Shabsigh R
CORPORATE SOURCE: Department of Urology, Columbia-Presbyterian Medical Center, 161 Fort Washington Avenue, New York, NY 10032, USA.. rs66@columbia.edu
SOURCE: Curr Psychiatry Rep, (2000 Jun) 2 (3) 196-200. Ref: 8
Journal code: 100888960. ISSN: 1523-3812.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020501
Entered Medline: 20020430

AB The past few years have witnessed major developments in the management of male sexual dysfunction. The introduction of the first efficacious and safe oral medication (sildenafil) resulted in the expansion of the patient base and, the change in health care delivery, with erectile dysfunction (ED) entering the primary care physician's practice. New guidelines for the diagnosis and treatment of ED have been developed, including the Process of Care in the USA and the 1st International Consultation on ED sponsored by the World Health Organization. Well-defined algorithms for diagnosis and treatment have been adopted. These recent developments have brought up challenging issues, including the cardiovascular safety of sexual activity, societal changes, internet prescriptions, definition of the patient, expansion of clinical and laboratory research, rise of interest in female sexual dysfunction, and a significant economic impact. The recent developments in male sexual dysfunction continue with the study of new oral medications. Some of these new medications, such as sublingual apomorphine, have a central mode of action, whereas others, such as the phosphodiesterase inhibitor **IC351**, have a selective peripheral vasodilation-enhancing action.

L25 ANSWER 44 OF 58 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-572170 [53] WPIDS
DOC. NO. CPI: C2000-170623
TITLE: New nitrosated and nitrosylated prostaglandins, useful for treating or preventing e.g. sexual dysfunction in males and females, cerebrovascular disorders and glaucoma.
DERWENT CLASS: B05
INVENTOR(S): GARVEY, D S; GASTON, R D; LETTS, G L; SAENZ DE TEJADA, I; TAM, S W; WORCEL, M
PATENT ASSIGNEE(S): (NITR-N) NITROMED INC
COUNTRY COUNT: 90
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 2000051978 | A1 | 20000908 | (200053)* | EN | 82 |

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000037136 A 20000921 (200065)

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 2000051978 A1 | | WO 2000-US5286 | 20000301 |
| AU 2000037136 A | | AU 2000-37136 | 20000301 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---|---|---|
| AU 2000037136 A | Based on | WO 200051978 |

PRIORITY APPLN. INFO: US 1999-138502P 19990609; US 1999-122273P 19990301

AB WO 200051978 A UPAB: 20001023

NOVELTY - Nitrosated and nitrosylated prostaglandins (I) and compositions comprising them are new, also compositions comprising a prostaglandin and S-nitrosothiol compound.

DETAILED DESCRIPTION - Nitrosated and nitrosylated prostaglandins of formula (I) are new:

bonds a', b', c', d' = single or double bonds;

R1 = -OD1 or Cl;

R2, R8 = H; or

R1+R2 = =CH2 or =O;

R3, R4 = H, -OD1 or Me;

R5, R6 = H, -OD1, Me, OMe or -CH=CH2;

R7 = H or OD1;

R9 = H or absent when the C to which it is attached is the central carbon of an allene; or

R8+R9+attached chain atoms = a substituted benzene ring provided that R1 is O which is attached to the C at the position of the benzene ring defined by B';

A = -CH=, -CH2-, -S- or -O-;

B' = -CH=, -CH2-, -S- or -C(O)-;

X = -CH2OR11, -C(O)OR11 or -C(O)N(D1)R12;

R11 = D1, 1-10C alkyl or a group of formula (i):

R12 = -S(O)2CH3 or -C(O)CH3;

Z' = ethyl, butyl, hexyl, benzyl, -CH2-O-CH2-CH3, -CH(CH3)-(CH2)3-CH3 or a group of formula (ii) or (iii):

R13 = H or Cl;

D1 = H or D; provided that at least 1 D1 is D;

D = Q or K;

Q = -NO or NO2;

K = -Wa-Eb-(C(Re)(Rf))p-Ec-(C(Re)(Rf))x-Wd -(C(Re)(Rf))y-Wi-Ej-Wg-(C(Re)(Rf))z-T-Q;

a, b, c, d, g, i, j = 0-3;

p, x, y, z = 0-10;

E = -T-, alkyl, aryl, (C(Re)(Rf))h-,

W = -C(O)-, -C(S)- or as defined for E;

h = 1 10;

q = 1-5;

Re, Rf = H, alkyl, cycloalkoxy, halo, OH, hydroxyalkyl, alkoxyalkyl, aryl-heterocyclic, alkylaryl, cycloalkylalkyl, heterocyclic-alkyl, alkoxy, haloalkoxy, NH2, alkylamino, dialkylamino, arylamino, diarylamino,

alkylarylamino, alkoxyhaloalkyl, haloalkoxy, sulfonic acid, sulfonic ester, alkylsulfonic acid, arylsulfonic acid, arylalkoxy, alkylthio, arylthio, cycloalkylthio, cycloalkenyl, CN, aminoalkyl, aminoaryl, aryl, arylalkyl, alkylaryl, carboxamido, alkylcarboxamido, arylcarboxamido, amidyl, carboxyl, carbamoyl, alkylcarboxylic acid, arylcarboxylic acid, alkylcarbonyl, arylcarbonyl, ester, carboxylic ester, alkylcarboxylic ester, arylcarboxylic ester, haloalkoxy, sulfonamido, alkylsulfonamido, arylsulfonamido, sulfonic ester, a urea, phosphoryl, nitro, -T-Q or -(C(Re)(Rf))k-T-Q; or

Re+Rf+attached C atoms = carbonyl, methanthial, heterocyclic, cycloalkyl or a bridged cycloalkyl;

k = 1-3;

T = a covalent bond, carbonyl, O, -S(O)o- or -N(Ra)Ri-;

o = 0-2;

Ra = a lone pair of electrons, H or alkyl;

Ri = H, alkyl, aryl, alkylcarboxylic acid, arylcarboxylic acid, alkylcarboxylic ester, arylcarboxylic ester, alkylcarboxamido, arylcarboxamido, alkylaryl, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, sulfonamido, carboxamido, carboxylic ester, amino alkyl, amino aryl, -CH2-C(T-Q)(Re)(Rf) or -(N2O2)-M+;

M+ = an organic or inorganic cation;

provided that when Ri is -CH2-C(T-Q)(Re)(Rf) or -(N2O2) M+; or Re or Rf are T-Q or (C(Re)(Rf))k-T-Q, then T-Q can be H, alkyl, alkoxy, alkoxyalkyl, aminoalkyl, OH, heterocyclic or aryl; and provided that when X is -C(O)OD1 and D1 is K, then K is not alkyl or cycloalkyl mononitrate; benzoic acid substituted benzyloxy mononitrate; ethylene glycol mononitrate; polyethylene glycol mononitrate; the regioisomeric esters of glycerol dinitrate and oligomers as disclosed in WO9858910.

INDEPENDENT CLAIMS are included for the following:

(a) compositions and kits comprising (I) and at least 1 compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase, and/or at least 1 vasoactive agent; and

(b) compositions and kits comprising at least 1 prostaglandin and at least 1 S-nitrosothiol compound, useful for treating sexual dysfunction, a cerebrovascular disorder, cardiovascular disorder, benign prostatic hyperplasia, organ transplants, glaucoma or peptic ulcer, or for inducing an abortion.

ACTIVITY - Vasotropic; Cerebroprotective; Cardiant; Cytostatic; Ophthalmological; Antiulcer; Gynecological; Relaxant.

MECHANISM OF ACTION - Smooth muscle relaxant; Nitric oxide donor; Endothelium-derived relaxing factor agonist.

USE - For treating or preventing sexual dysfunction in males or females, treating a cerebrovascular disorder, cardiovascular disorder, benign prostatic hyperplasia, organ transplants, glaucoma or peptic ulcer, or for inducing an abortion (all claimed).

ADVANTAGE - The combination of a prostaglandin and a S-nitrosothiol gives synergistic results.

Dwg.0/4

L25 ANSWER 45 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:355438 BIOSIS
DOCUMENT NUMBER: PREV200200355438
TITLE: Efficacy and safety of **tadalafil** in men with erectile dysfunction with and without hypertension.
AUTHOR(S): Padma-Nathan, H. (1); Brock, G.; McMahon, C.; Chen, K. K.; Anglin, G.; Costigan, T.; Shen, W.; Watkins, V.; Whitaker, J. S.
CORPORATE SOURCE: (1) Keck School of Medicine, University of Southern California, Beverly Hills, CA USA

SOURCE: American Journal of Hypertension, (April, 2002) Vol. 15, No. 4 Part 2, pp. 143A-144A. http://www.ajh-us.org. print.
Meeting Info.: Seventeenth Annual Scientific Meeting of the American Society of Hypertension New York, N.Y., USA May 14-18, 2002
ISSN: 0895-7061.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 46 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:355428 BIOSIS
DOCUMENT NUMBER: PREV200200355428
TITLE: Blood pressure and cardiovascular effects of **tadalafil**, a new PDE5 inhibitor.
AUTHOR(S): Hutter, A. M. (1); Kloner, R. A.; Watkins, V.; Costigan, T.; Bedding, A.; Mitchell, M.; Emmick, J.
CORPORATE SOURCE: (1) Massachusetts General Hospital, Harvard Medical School, Boston, MA USA
SOURCE: American Journal of Hypertension, (April, 2002) Vol. 15, No. 4 Part 2, pp. 140A. http://www.ajh-us.org. print.
Meeting Info.: Seventeenth Annual Scientific Meeting of the American Society of Hypertension New York, N.Y., USA May 14-18, 2002
ISSN: 0895-7061.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 47 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:449004 BIOSIS
DOCUMENT NUMBER: PREV200100449004
TITLE: CialisTM (**IC351**) as a treatment of erectile dysfunction in diabetic men.
AUTHOR(S): Saenz De Tejada, Inigo (1); Fredlund, Paul (1); Anglin, Greg (1); Pullman, Bill (1); Emmick, Jeff (1)
CORPORATE SOURCE: (1) Madrid Spain
SOURCE: Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A425. print.
Meeting Info.: 61st Scientific Sessions of the American Diabetes Association Philadelphia, Pennsylvania, USA June 22-26, 2001
ISSN: 0012-1797.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 48 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:380171 BIOSIS
DOCUMENT NUMBER: PREV200100380171
TITLE: CialisTM (**IC351**) provides prompt response and extended period of responsiveness for the treatment of men with erectile dysfunction (ED.
AUTHOR(S): Padma-Nathan, Harin (1); Rosen, Raymond C.; Shabsigh, Ridwan; Saikali, Khalil; Watkins, Vish S.; Pullman, Bill
CORPORATE SOURCE: (1) Los Angeles, CA USA
SOURCE: Journal of Urology, (May, 2001) Vol. 165, No. 5 Supplement, pp. 224. print.
Meeting Info.: Annual Meeting of the American Urological Association, Inc. Anaheim, California, USA June 02-07, 2001
ISSN: 0022-5347.
DOCUMENT TYPE: Conference
LANGUAGE: English

SUMMARY LANGUAGE: English

L25 ANSWER 49 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:381536 BIOSIS
DOCUMENT NUMBER: PREV200100381536
TITLE: Cellular localisation of phosphodiesterase type 11 (PDE11) in human corpus cavernosum and the contribution of PDE11 inhibition on nerve-stimulated relaxation.
AUTHOR(S): Baxendale, Rhona W. (1); Wayman, Christopher P. (1); Turner, Leigh (1); Phillips, Stephen C. (1)
CORPORATE SOURCE: (1) Sandwich UK
SOURCE: Journal of Urology, (May, 2001) Vol. 165, No. 5 Supplement, pp. 223-224. print.
Meeting Info.: Annual Meeting of the American Urological Association, Inc. Anaheim, California, USA June 02-07, 2001
ISSN: 0022-5347.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 50 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:262700 BIOSIS
DOCUMENT NUMBER: PREV200100262700
TITLE: CialisTM (**IC351**): Effective and well-tolerated treatment for ED.
AUTHOR(S): Brock, G. (1); Iglesias, J.; Toulouse, K.; Ferguson, K.; Pullman, W.; Anglin, G.
CORPORATE SOURCE: (1) Univ W Ontario, London, ON Canada
SOURCE: Journal of Andrology, (May June, 2001) No. Supplement, pp. 185. print.
Meeting Info.: VIIth International Congress of Andrology Montreal, Canada June 15-19, 2001
ISSN: 0196-3635.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 51 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:389604 BIOSIS
DOCUMENT NUMBER: PREV200100389604
TITLE: Efficacy and safety of **IC351** treatment for ED.
AUTHOR(S): Brock, G. (1); Iglesias, J.; Toulouse, K.; Ferguson, K.; Pullman, W.; Anglin, G.
CORPORATE SOURCE: (1) Univ. of W. Ontario, London, ON Canada
SOURCE: European Urology, (March, 2001) Vol. 39, No. Suppl. 5, pp. 106. print.
Meeting Info.: XVIth Congress of the European Association of Urology Geneva, Switzerland April 07-10, 2001
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 52 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:391998 BIOSIS
DOCUMENT NUMBER: PREV200100391998
TITLE: **IC351** enhances NO-mediated relaxation of human arterial and trabecular penile smooth muscle.
AUTHOR(S): Angulo, J. (1); Gadau, M.; Fernandez, A.; Gabancho, S.; Cuevas, P.; Martins, T.; Florio, V.; Ferguson, K.; Saenz De Tejada, I.

CORPORATE SOURCE: (1) Hospital Ramon y Cajal, Madrid Spain
SOURCE: European Urology, (March, 2001) Vol. 39, No. Suppl. 5, pp. 106. print.
Meeting Info.: XVIth Congress of the European Association of Urology Geneva, Switzerland April 07-10, 2001
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 53 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:375151 BIOSIS
DOCUMENT NUMBER: PREV200100375151
TITLE: The effect of on-demand **IC351** treatment of erectile dysfunction in men with diabetes.
AUTHOR(S): Saenz De Tejada, Inigo (1); Emmick, J.; Anglin, G.; Fredlund, P.; Pullman, W.
CORPORATE SOURCE: (1) Hospital Ramon y Cajal, Madrid Spain
SOURCE: European Urology, (March, 2001) Vol. 39, No. Suppl. 5, pp. 16. print.
Meeting Info.: XVIth Congress of the European Association of Urology Geneva, Switzerland April 07-10, 2001
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 54 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:211709 BIOSIS
DOCUMENT NUMBER: PREV200000211709
TITLE: Daily and on-demand **IC351** treatment of erectile dysfunction.
AUTHOR(S): Giuliano, Francois (1); Porst, Hartmut; Padma-Nathan, Harin; Saoud, Jay; Ferguson, Kenneth; Whitaker, Steven; Pullman, William; Rosen, Raymond
CORPORATE SOURCE: (1) Bicetre France
SOURCE: Journal of Urology, (April, 2000) Vol. 163, No. 4 Suppl., pp. 201.
Meeting Info.: 95th Annual Meeting of the American Urological Association, Inc. Atlanta, Georgia, USA April 29, 2000-May 04, 1999
ISSN: 0022-5347.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 55 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:356087 BIOSIS
DOCUMENT NUMBER: PREV200000356087
TITLE: On-demand treatment of erectile dysfunction with **IC351**.
AUTHOR(S): Padma-Nathan, Harin (1); McMurray, James; Saoud, Jay; Ferguson, Kenneth; Pullman, William; Whitaker, Steven; Rosen, Raymond
CORPORATE SOURCE: (1) Male Clinic, University of Southern California, Santa Monica, CA USA
SOURCE: European Urology, (March, 2000) Vol. 37, No. Suppl. 2, pp. 80. print.
Meeting Info.: XVth Congress of the European Association of Urology Brussels, Belgium April 12-15, 2000
ISSN: 0302-2838.

DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 56 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:356088 BIOSIS
DOCUMENT NUMBER: PREV200000356088
TITLE: Daily **IC351** treatment of erectile dysfunction.
AUTHOR(S): Giuliano, Francois (1); Meuleman, Eric; Saoud, Jay; Ferguson, Kenneth; Whitaker, Steven; Porst, Hartmut
CORPORATE SOURCE: (1) Department of Urology, University Hospital of Bicetre, Le Kremlin France
SOURCE: European Urology, (March, 2000) Vol. 37, No. Suppl. 2, pp. 80. print.
Meeting Info.: XVth Congress of the European Association of Urology Brussels, Belgium April 12-15, 2000
ISSN: 0302-2838.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L25 ANSWER 57 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:160377 BIOSIS
DOCUMENT NUMBER: PREV199900160377
TITLE: Effects of **IC351** on erectile response to visual sexual stimulation.
AUTHOR(S): Meuleman, Eric; Nijeholt, Guus Lycklama A; Slob, Koos; Roeleveld; Damen, Lianne; Brazao, Gouveia De C.; Harin, Padma-Nathan; Rosen, Raymond
CORPORATE SOURCE: Nijmegen Netherlands
SOURCE: Journal of Urology, (April, 1999) Vol. 161, No. 4 SUPPL., pp. 212.
Meeting Info.: 94th Annual Meeting of the American Urological Association, Inc. Dallas, Texas, USA May 1-6, 1999 American Urological Association
. ISSN: 0022-5347.
DOCUMENT TYPE: Conference
LANGUAGE: English

L25 ANSWER 58 OF 58 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1980:167480 BIOSIS
DOCUMENT NUMBER: BA69:42476
TITLE: CYTO GENETIC STUDIES ON FISHES 2. KARYOTYPES OF 4 CARANGID FISHES.
AUTHOR(S): MUROFUSHI M; YOSIDA T H
CORPORATE SOURCE: LAB. BIOL., MISHIMA JR. COLL., NIHON UNIV., MISHIMA, TOKYO 411, JPN.
SOURCE: JPN J GENET, (1979) 54 (5), 367-370.
CODEN: IDZAAW. ISSN: 0021-504X.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB All Trachurus japonicus, Caranx equula, C. sexfasciatus and Alectis **cialis** all had a diploid chromosome number of 48. The karotype consisted of all acrocentric chromosomes (no. 1-24) in A. cilialis, but the largest chromosome pair no. 1 was subtelocentric in C. equula and C. sexfasciatus. In T. japonicus the karyotype was different from the other species by consisting of 15 biarmed chromosome pairs (no. 1-15) and 9 acrocentric pairs (no. 16-24). The sex chromosomes cannot be identified in any of the 4 spp. studied. The relationship between karyotype differentiation and species diversity of carangid fishes was discussed.

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